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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7: C12N 15/11, C07H 21/00, C12N 15/31, C07K 14/195, 16/12 (11) International Publication Number:

WO 00/18909

(43) International Publication Date:

6 April 2000 (06.04.00)

(21) International Application Number:

PCT/US99/22752

(22) International Filing Date:

29 September 1999 (29.09.99)

(30) Priority Data:

60/102,294

29 September 1998 (29.09.98) US

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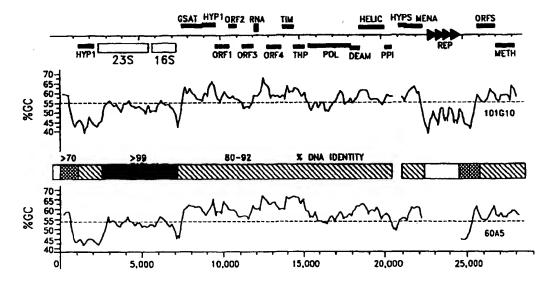
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Published

Without international search report and to be republished upon receipt of that report.

IDN:47 94.6 Claim 15

(54) Title: NUCLEIC ACIDS AND PROTEINS FROM CENARCHAEUM SYMBIOSUM



(57) Abstract

The present application relates to nucleic acids and polypeptides from Cenarchaeum symbiosum. Methods of making the polypeptides and antibodies against the polypeptides are also described.

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NUCLEIC ACIDS AND PROTEINS FROM CENARCHAEUM SYMBIOSUM

Background of the Invention

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The identification and characterization of organisms which inhabit a diverse range of ecosystems leads to a greater understanding of the operation of such ecosystems. In addition, because the physiology of such organisms is adapted to function in the particular habitat which the organism inhabits, the enzymes which carry out the organism's physiological processes may possess characteristics which provide advantages when they are utilized in therapeutic procedures, industrial applications, or research applications. Furthermore, by determining the sequences of these organisms' genes, insight into their biochemical pathways and processes may be gained without the necessity of culturing the organisms in the laboratory, thereby enabling the physiological characterization of organisms which are recalcitrent to growth in the laboratory.

Molecular phylogenetic surveys have recently revealed an ecologically widespread Crenarchaeal group that inhabits cold and temperate terrestrial and marine environments. To date these organisms have resisted isolation in pure culture, so their phenotypic and genotypic characteristics remain largely unknown. In order to characterize the physiology of these archaea, to develop methodological approaches for characterizing uncultivated microorganisms and identifying their presence in a sample, and to identify enzymes produced by these archae which may be useful in therapeutic, industrial, or laboratory applications, genomic analyses of the non-thermophilic crenarchaeote

Cenarchaeum symbiosum was undertaken.

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Non-thermophilic Crenarchaeota are one of the more abundant, widespread and frequently recovered prokaryotic groups revealed by molecular phylogenetic approaches. These microorganisms were originally detected in high abundance in temperate ocean waters and polar seas. (DeLong, E. F. 1992. Archaea in coastal marine environments. Proc. Natl. Acad. Sci. 89, 5685-5689; DeLong, E. F et al. 1994. High abundance of Archaea in Antarctic marine picoplankton. Nature 371, 695-697; Fuhrman, J. A., et al. Davis. 1992. Novel major archaebacterial group from marine plankton. Nature 356, 148-149; Massana, R., et al. 1997. Vertical distribution and phylogenetic characterization of marine planktonic Archaea in the Santa Barbara Channel. Appl. Env. Microb. 63, 50-56; McInerney, J.O. et al. 1995. Recovery and phylogenetic analysis of novel archaeal rRNA sequences from a deep-sea deposit feeder. Appl. Env. Microb. 61, 1646-1648; Preston, C. M. et al. 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. Proc. Natl. Acad. Sci. USA 93, 6241-6246) Representatives have now been reported in terrestrial environments and freshwater lake sediments, indicating a widespread distribution. (Bintrim, S.B. et al. 1997. Molecular phylogeny of Archaea from soil. Proc. Natl. Acad. Sci. USA 94, 277-282; Jurgens, G. et al. 1997. Novel group within the kingdom Crenarchaeota from boreal forest soil. Appl. Env. Mircob. 63, 803-80515, Kudo, Y. et al. 1997. Peculiar archaea found in Japanese paddy soils. Biosc. Biotech. Biochem. 61, 917-920; Ueda, et al. 1995. Molecular phylogenetic analysis of a soil microbial community. Eur. J. Soil Sci. 46, 415-421; Hershberger, K. L. et al. 1996. Wide diversity of Crenarchaeota. Nature 384, 420;

MacGregor, B.J. 1997. Crenarchaeota in Lake Michigan sediment. *Appl. Env. Microb.* 63, 1178-1181 *et al.*; Schleper, C.*et al.* 1997. Recovery of crenarchaeotal ribosomal DNA sequences from freshwater-lake sediments. *Appl. Env. Microb.* 63, 321-323) The ecological distribution of these organisms was initially surprising, since their closest cultivated relatives are all thermophilic or hyperthermophilic. No representative of this new archaeal group has yet been obtained in pure culture, so the phenotypic and metabolic properties of these organisms, as well as their impact on the environment and global nutrient cycling, remain unknown. Since growth temperature and habitat characteristics vary so widely between non-thermophilic and the hyperthermophilic *Creanarchaeota*, these groups are likely to differ greatly with respect to their specific physiology and metabolism.

To gain a better perspective on the genetic and physiological characteristics of non-thermophilic crenarchaeotes, a genomic study of *Cenarchaeum symbiosum* was begun. This archaeon lives in specific association with the marine sponge *Axinella mexicana* off the coast of California, allowing access to relatively large amounts of biomass from this species. (Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA **93**, 6241-6246) The approach taken herein differs in several respects from now standard genomic characterization of cultivated organisms, and also from comparable studies of uncultivated obligate parasites or symbionts. *C. symbiosum* has not been completely physically separated from the tissues of its metazoan host. Therefore, its genetic material needs to be identified within the context of complex genomic libraries that contain significant amounts of eucaryotic DNA, as well as DNA derived from members of *Bacteria*.

Molecular phylogenetic surveys of mixed microbial populations have revealed the existence of many new lineages undetected by classical microbiological approaches. (DeLong, E. F. 1997. Marine microbial diversity: the tip of the iceberg. *Tibtech* 15, 2-9.; Pace, N. R. 1997. A molecular view of microbial diversity and the biosphere. *Science* 276, 734-740) Furthermore, quantitative rRNA hybridization experiments demonstrate that some of these novel prokaryotic groups represent major components of natural microbial communities. These molecular phylogenetic approaches have altered current views of microbial diversity and ecology, and have demonstrated that traditional cultivation techniques may recover only a small, skewed fraction of naturally occurring microbes. However, phylogenetic identification using single gene sequences provides a limited perspective on other biological properties, particularly for novel lineages only distantly related to cultivated and characterized organisms. Consequently, additional approaches are necessary to better characterize ecologically abundant and potentially biotechnologically useful microorganisms, many of which resist cultivation attempts.

Summary of the Invention

One embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2, the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2, fragments comprising at least 10 consecutive nucleotides of SEQ ID NO: 1 and SEQ ID NO: 2, and fragments comprising at least 10 consecutive nucleotides of the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of

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hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEO ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis

with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

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Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to the polypeptide of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to the polypeptide of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide comprising at least 10 and 10 polypeptide to 10 polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide comprising at least 10 polypeptide polypeptide of 10 polypeptide 10 polypeptide comprising at least 10 polypeptide polypeptide 10 polypeptid

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consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters.

Another aspect of the present invention is an isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 58, 70, 74, and 78. One aspect of the present invention is an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is An isolated or purified polypeptide having at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to an isolated or purified polypeptide comprising at least 99% homology to an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is a method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

Another embodiment of the present invention is a method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

Another embodiment of the present invention is a method of making a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

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Another embodiment of the present invention is a method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

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Another embodiment of the present i method of generating a variant comprising obtaining a nucleic acid comprising a sequence selected from the group consisting of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, the sequences complementary to the sequences of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments comprising at least 30 consecutive nucleotides of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEO ID NOS. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and 61, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and changing one or more nucleotides in said sequence. In one aspect of the present invention, the method further comprises the step of testing the enzymatic properties of a translation product of said variant.

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Another embodiment of the present invention is a computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 86, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

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Another embodiment of the present invention is a computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. In one aspect of the present invention, the computer system further comprises a sequence comparer and a data storage device having reference sequences stored thereon. For example, the sequence comparer may comprise a computer program which indicates polymorphisms. In another aspect of the present invention is the computer system of this embodiment further comprises an identifier which identifies features in said sequence.

Another embodiment of the present invention is a method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 48, 58, 60, 62, 84, 68, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of reading said first sequence and said reference sequence through use of a computer program which compares sequences; and determining differences between said first sequence and said reference sequence with said computer program. In one aspect of the present invention, the step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.

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Another embodiment of the present invention is a method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63. 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of reading said sequence through the use of a computer program which identifies features in sequences and identifying features in said sequence with said computer program.

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Brief Description of the Drawings

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Figure 1 shows the locations of coding regions, the %G-C. and the %DNA identity between the approximately 28Kb of common sequence in fosmids 101G10 and 60A5.

Figure 2 shows the sequences surrounding the TATA boxes of several promoters from Cenarchaeum symbiosum and the distances from the TATA boxes to the initiation codons in these sequences.

Figure 3 is a block diagram of an exemplary computer system.

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Figure 4 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database.

Figure 5 is a flow diagram illustrating one embodiment of a process 250 in a computer for determining whether two sequences are homologous.

Figure 6 is a flow diagram illustrating one embodiment of an identifier process for detecting the presence of

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a feature in a sequence.

Definitions

The term "gene" means the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding region (leader and trailer) as well as, where applicable, intervening sequences (introns) between individual coding segments (exons).

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As used herein, the term "isolated" means that the material is removed from its original environment (e.g.,

the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of its natural environment.

As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual nucleic acids obtained from a library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The purified nucleic acids of the present invention have been purified from the remainder of the genomic DNA in the organism by at least 10⁴-10⁶ fold. However, the term "purified" also includes nucleic acids which have been purified from the remainder of the genomic DNA or from other sequences in a library or other environment by at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude.

As used herein, the term "recombinant" means that the nucleic acid is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the nucleic acids will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched nucleic acids represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched nucleic acids represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched nucleic acids represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules.

A promoter sequence is "operably linked to" a coding sequence when RNA polymerase which initiates transcription at the promoter will transcribe the coding sequence into mRNA.

"Recombinant" polypeptides or proteins refer to polypeptides or proteins produced by recombinant DNA techniques; *i.e.*, produced from cells transformed by an exogenous DNA construct encoding the desired polypeptide or protein. "Synthetic" polypeptides or protein are those prepared by chemical synthesis.

A DNA "coding sequence" or a "nucleotide sequence encoding" a particular polypeptide or protein, is a DNA sequence which is transcribed and translated into a polypeptide or protein when placed under the control of appropriate regulatory sequences.

"Plasmids" are designated by a lower case p preceded and/or followed by capital letters and/or numbers. The starting plasmids herein are either commercially available, publicly available on an unrestricted basis, or can be constructed from available plasmids in accord with published procedures. In addition, equivalent plasmids to those described herein are known in the art and will be apparent to the ordinarily skilled artisan.

"Digestion" of DNA refers to catalytic cleavage of the DNA with a restriction enzyme that acts only at

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certain sequences in the DNA. The various restriction enzymes used herein are commercially available and their reaction conditions, cofactors and other requirements were used as would be known to the ordinarily skilled artisan. For analytical purposes, typically 1 g of plasmid or DNA fragment is used with about 2 units of enzyme in about 20 l of buffer solution. For the purpose of isolating DNA fragments for plasmid construction, typically 5 to 50 g of DNA are digested with 20 to 250 units of enzyme in a larger volume. Appropriate buffers and substrate amounts for particular restriction enzymes are specified by the manufacturer. Incubation times of about 1 hour at 37 C are ordinarily used, but may vary in accordance with the supplier's instructions. After digestion the gel electrophoresis may be performed to isolate the desired fragment.

"Oligonucleotide" refers to either a single stranded polydeoxynucleotide or two complementary polydeoxynucleotide strands which may be chemically synthesized. Such synthetic oligonucleotides have no 5' phosphate and thus will not ligate to another oligonucleotide without adding a phosphate with an ATP in the presence of a kinase. A synthetic oligonucleotide will ligate to a fragment that has not been dephosphorylated.

Detailed Description of the Preferred Embodiment

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In order to begin the characterization of *Cenarchaeum symbiosum*, a large region of the *C. symbiosum* genome was sequenced. In particular, two overlapping *C. symbiosum*-derived fosmid inserts of approximately 42kb and 33kb were sequenced. The sequences of the two fosmid inserts revealed that there are at least two major variants or strains of *C. symbiosum* that coexist inside the sponge tissues of a single sponge. This complexity of the *C. symbiosum* population was not detected in initial studies based solely on direct sequencing of PCR amplified SSU genes. (Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6246) This natural variation would also have been lost upon isolation of a pure culture.

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The Cenarchaeum symbiosum sequences obtained from the two fosmids containing overlapping genomic inserts are provided in the accompanying sequence listing and are identified as SEQ ID NO: 1 and SEQ ID NO: 2. The two fosmid sequences were not entirely identical in their overlapping portions but instead contained differences. Upon further investigation, it was discovered that the two fosmid sequences were derived from two different, but closely related, strains of Cenarchaeum symbiosum (called variant A and variant B) which may simultaneously inhabit a single sponge.

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Within the sequences of the fosmid inserts, numerous open reading frames encoding polypeptides having homology to known proteins, as well as open reading frames encoding proteins which do not exhibit homology to known proteins, were identified. Homology was determined using the program FASTA with the default parameters. The polypeptides encoded by these sequences are identified in the accompanying sequence listing as SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76 and 80 (polypeptides with homology to known proteins) and SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74 and 78 (polypeptides

without homology to known proteins). In addition, sequences encoding the 16S rRNA, the 23S rRNA and a tyrosine tRNAs were also identified.

One aspect of the present invention is an isolated, purified, or enriched nucleic acid comprising one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto. The isolated, purified or enriched nucleic acids may comprise DNA, including cDNA, genomic DNA, and synthetic DNA. The DNA may be double-stranded or single-stranded, and if single stranded may be the coding strand or non-coding (anti-sense) strand. Alternatively, the isolated, purified or enriched nucleic acids may comprise RNA.

As discussed in more detail below, the isolated, purified, or enriched nucleic acids of one of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 may be used to prepare one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80.

Accordingly, another aspect of the present invention is an isolated, purified, or enriched nucleic acid which encodes one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80. The coding sequences of these nucleic acids may be identical to one of the coding sequences of one of the nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or a fragment thereof or may be different coding sequences which encode one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments code. The genetic code is well known to those of skill in the art and can be obtained, for example, on page 214 of B. Lewin, Genes VI, Oxford University Press, 1997.

The isolated, purified, or enriched nucleic acid which encodes one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68,

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70, 72, 74 76, 78, and 80 may include, but is not limited to: only the coding sequence of one of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79; the coding sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 8, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 and additional coding sequences, such as leader sequences or proprotein sequences; or the coding sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 and non-coding sequences, such as introns or non-coding sequences 5' and/or 3' of the coding sequence. Thus, as used herein, the term "polynucleotide encoding a polynucleotide which includes only coding sequence for the polypeptide as well as a polynucleotide which includes additional coding and/or non-coding sequence.

Alternatively, the nucleic acid sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 may be mutagenized using conventional techniques, such as site directed mutagenesis, or other techniques familiar to those skilled in the art, to introduce silent changes into the polynucleotides of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79. As used herein, "silent changes" include, for example, changes which do not alter the amino acid sequence encoded by the polynucleotide. Such changes may be desirable in order to increase the level of the polypeptide produced by host cells containing a vector encoding the polypeptide by introducing codons or codon pairs which occur frequently in the host organism.

The present invention also relates to polynucleotides which have nucleotide changes which result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80. Such nucleotide changes may be introduced using techniques such as site directed mutagenesis, random chemical mutagenesis, exonuclease III deletion, and other recombinant DNA techniques. Alternatively, such nucleotide changes may be naturally occurring allelic variants which are isolated by identifying nucleic acids which specifically hybridize to probes comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto to nucleic acids from *Cenarchaeum symbiosum* or related organisms under conditions of high, moderate, or low strigency as provided herein.

The isolated, purified, or enriched nucleic acids of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77

and 79 or the sequences complementary thereto may also be used as probes to identify the presence of *Cenarchaeum symbiosum* in a biological sample. In such procedures, a biological sample potentially harboring *Cenarchaeum symbiosum* is obtained and nucleic acids are obtained from the sample. The nucleic acids are contacted with the probe under conditions which permit the probe to specifically hybridize to any complementary sequences from *Cenarchaeum symbiosum* which are present therein.

Where necessary, conditions which permit the probe to specifically hybridize to complementary sequences from *Cenarchaeum symbiosum* may be determined by placing the probe in contact with complementary sequences from *Cenarchaeum symbiosum* as well as control sequences which are not from *Cenarchaeum symbiosum*. In some analyses, the control sequences may be from organisms related to *Cenarchaeum symbiosum*. Alternatively, the control sequences may be from organisms which are not related to *Cenarchaeum symbiosum*. Hybridization conditions, such as the salt concentration of the hybridization buffer, the formamide concentration of the hybridization buffer, or the hybridization temperature, may be varied to identify conditions which allow the probe to hybridize specifically to nucleic acids from *Cenarchaeum symbiosum*.

If the sample contains nucleic acids from *Cenarchaeum symbiosum*, specific hybridization of the probe to the nucleic acids from *Cenarchaeum symbiosum* is then detected. Hybridization may be detected by labeling the probe with a detectable agent such as a radioactive isotope, a fluorescent dye or an enzyme capable of catalyzing the formation of a detectable product.

Many methods for using the labeled probes to detect the presence of nucleic acids from *Cenarchaeum symbiosum* in a sample are familiar to those skilled in the art. These include Southern Blots, Northern Blots, colony hybridization procedures, and dot blots. Protocols for each of these procedures are provided in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989.

Alternatively, more than one probe (at least one of which is capable of specifically hybridizing to any complementary sequences from *Cenarchaeum symbiosum* which are present in the nucleic acid sample), may be used in an amplification reaction to determine whether the nucleic acid sample contains nucleic acids from *Cenarchaeum symbiosum*. Preferably, the probes comprise oligonucleotides. In one embodiment, the amplification reaction may comprise a PCR reaction. PCR protocols are described in Ausubel and Sambrook, *supra*. Alternatively, the amplification may comprise a ligase chain reaction, 3SR, or strend displacement reaction. (See Barany, F., "The Ligase Chain Reaction in a PCR World", *PCR Methods and Applications* 1:5-16 (1991); E. Fahy *et al.*, "Self-sustained Sequence Replication (3SR): An Isothermal Transcription-based Amplification System Alternative to PCR", *PCR Methods and Applications* 1:25-33 (1991); and Walker G.T. *et al.*, "Strand Displacement Amplification-an Isothermal *in vitro* DNA Amplification Technique, *Nucleic Acid Research* 20:1691-1696 (1992). In such procedures, the nucleic acids in the sample are contacted with the probes, the amplification reaction is performed, and any resulting amplification product is detected. The amplification product may be detected by performing gel electrophoresis on the reaction products and staining the gel with an interculator such as ethicium bromide. Alternatively, one or more of the probes may be labeled with a radioactive

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isotope and the presence of a radioactive amplification product may be detected by autoradiography after gel electrophoresis.

Probes derived from sequences near the ends of the sequences of SEQ ID Nos: 1 and 2 may also be used in chromosome walking procedures to identify clones containing genomic sequences located adjacent to the sequences of SEQ ID Nos: 1 and 2. Such methods allow the isolation of genes which encode additional proteins expressed in Cenarchaeum symbiosum and facilitate the further physiological characterization of the organism.

Another aspect of the present invention is a method for determining whether a sample contains variant A and/or variant B of Cenarchaeum symbiosum. In such procedures, a sample potentially harboring variant A and/or variant B Cenarchaeum symbiosum is obtained and nucleic acids are obtained from the sample. The nucleic acids are contacted with the probe under conditions which permit the probe to specifically hybridize to any complementary sequences from variant A or variant B of Cenarchaeum symbiosum which are present therein. Preferably, the probe comprises a sequence having one or more nucleotides which differ between variant A and variant B. Conditions in which the probe specifically hybridizes to nucleic acids from one of the variants but not to nucleic acids from the other variant may be determined by contacting the probe with its corresponding sequence from variant A and variant B and varying the hybridization conditions, such as the salt concentration of the hybridization buffer, the formamide concentration of the buffer, or the hybridization temperature, to identify conditions in which the probe hybridizes to the corresponding sequence from one variant but not to the corresponding sequence from the other variant. Hybridization of the probe to nucleic acids from the Cenarchaeum symbiosum variant is then detected using any of the procedures described above.

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The isolated, purified, or enriched nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto may be used as probes to identify and isolate cDNAs encoding the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50. 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80. In such procedures, a cDNA library is constructed from a sample containing Cenarchaeum symbiosum. The cDNA library is then contacted with a probe comprising a coding sequence, or a fragment of a coding sequence, encoding one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment thereof under conditions which permit the probe to specifically hybridize to sequences complementary thereto. cDNAs which hybridize to the probe are then detected and isolated. Procedures for preparing and identifying cDNAs are disclosed in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989.

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The isolated, purified, or enriched nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto may be used as probes to identify and isolate related nucleic acids. In some embodiments, the related nucleic acids may be cDNAs or genomic DNAs from organisms other than *Cenarchaeum symbiosum*. For example, the other organisms may be organisms which are related to *Cenarchaeum symbiosum*. In such procedures, a nucleic acid sample containing nucleic acids from the related organism, such as a cDNA or genomic DNA library from the related organism, is contacted with the probe under conditions which permit the probe to specifically hybridize to related sequences. Hybridization of the probe to nucleic acids from the related organism is then detected using any of the methods described above.

Hybridization may be carried out under conditions of low stringency, moderate stringency or high stringency. As an example of nucleic acid hybridization, a polymer membrane containing immobilized denatured nucleic acids is first prehybridized for 30 minutes at 45 C in a solution consisting of 0.9 M NaCl, 50 mM NaH₂PO₄, pH 7.0, 5.0 mM Na₂EDTA, 0.5% SDS, 10X Denhardt's, and 0.5 mg/ml polyriboadenylic acid. Approximately 2 X 10⁷ cpm (specific activity 4-9 X 10⁸ cpm/ug) of ³²P end-labeled oligonucleotide probe are then added to the solution. After 12-16 hours of incubation, the membrane is washed for 30 minutes at room temperature in 1X SET (150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na₂EDTA) containing 0.5% SDS, followed by a 30 minute wash in fresh 1X SET at Tm-10 C for the oligonucleotide probe. The membrane is then exposed to auto-radiographic film for detection of hybridization signals.

By varying the stringency of the hybridization conditions used to identify nucleic acids, such as cDNAs or genomic DNAs, which hybridize to the detectable probe, nucleic acids having different levels of homology to the probe can be identified and isolated. Stringency may be varied by conducting the hybridization at varying temperatures below the melting temperatures of the probes. The melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm = 81.5 + 16.6(log [Na+]) + 0.41(fraction G + C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation $Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)\cdot(0.63\% formamide)\cdot(600/N)$ where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 g denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 g denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook et al., *supra*.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is

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contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25 C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 5-10 C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68 C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42 C.

All of the foregoing hybridizations would be considered to be under conditions of high stringency.

Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Nucleic acids which have hybridized to the probe are identified by autoradiography or other conventional techniques.

The above procedure may be modified to identify nucleic acids having decreasing levels of homology to the probe sequence. For example, to obtain nucleic acids of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5 C from 68 C to 42 C in a hybridization buffer having a Na+ concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50 C and "low" conditions below 50 C. A specific example of "moderate" hybridization conditions is when the above hybridization is conducted at 55 C. A specific example of "low stringency" hybridization conditions is when the above hybridization is conducted at 45 C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42 C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50 C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide. A specific example of "moderate" hybridization conditions is when the above hybridization is conducted at 30% formamide. A specific example of "low stringency" hybridization conditions is when the above hybridization is conducted at 10% formamide.

Nucleic acids which have hybridized to the probe are identified by autoradiography.

For example, the preceding methods may be used to isolate nucleic acids having a sequence with at least 97%, at least 95%, at least 85%, at least 80%, or at least 70% homology to a nucleic acid sequence selected from the group consisting of one of the sequences of SEO ID NOS. 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto. Homology may be measured using BLASTN version 2.0

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with the default parameters. For example, the homologous polynucleotides may have a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto.

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Additionally, the above procedures may be used to isolate nucleic acids which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, or at least 70% homology to a polypeptide having the sequence of one of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters.

Another aspect of the present invention is an isolated or purified polypeptide comprising the sequence of one of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. As discussed above, such polypeptides may be obtained by inserting a nucleic acid encoding the polypeptide into a vector such that the coding sequence is operably linked to a sequence capable of driving the expression of the encoded polypeptide in a suitable host cell. For example, the expression vector may comprise a promoter, a ribosome binding site for translation initiation and a transcription terminator. The vector may also include appropriate sequences for amplifying expression.

Promoters suitable for expressing the polypeptide or fragment thereof in bacteria include the $\underline{E.~coli.~lac}$ or \underline{trp} promoters, the lacl promoter, the lacZ promoter, the T3 promoter, the T7 promoter, the gpt promoter, the lambda P_R promoter, the lambda P_L promoter the trp promoter, promoters from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), and the acid phosphatase promoter. Fungal promoters include the α factor promoter. Eukaryotic promoters include the CMV immediate early promoter, the HSV thymidine kinase promoter, heat shock promoters, the early and late SV40 promoter, LTRs from retroviruses, and the mouse metallothionein-I promoter. Other promoters known to control expression of genes in prokaryotic or eukaryotic cells or their viruses may also be used.

Mammalian expression vectors may also comprise an origin of replication, any necessary ribosome binding sites, a polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. In some embodiments, DNA sequences derived from the SV4O splice and polyadenylation sites may be used to provide the required nontranscribed genetic elements.

Vectors for expressing the polypeptide or fragment thereof in eukaryotic cells may also contain enhancers to increase expression levels. Enhancers are cis-acting elements of DNA, usually from about 10 to about 300 bp in length that act on a promoter to increase its transcription. Examples include the SV40 enhancer on the late side of the

replication origin bp 100 to 270, the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and the adenovirus enhancers.

In addition, the expression vectors preferably contain one or more selectable marker genes to permit selection of host cells containing the vector. Such selectable markers include genes encoding dihydrofolate reductase or genes conferring neomycin resistance for eukaryotic cell culture, genes conferring tetracycline or ampicillin resistance in <u>E. coli</u>, and the <u>S. cerevisiae</u> TRP1 gene.

In some embodiments, the nucleic acid encoding one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof is assembled in appropriate phase with a leader sequence capable of directing secretion of the translated polypeptide or fragment thereof. Optionally, the nucleic acid can encode a fusion polypeptide in which one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof is fused to heterologous peptides or polypeptides, such as N-terminal identification peptides which impart desired characteristics, such as increased stability or simplified purification.

The appropriate DNA sequence may be inserted into the vector by a variety of procedures. In general, the DNA sequence is ligated to the desired position in the vector following digestion of the insert and the vector with appropriate restriction endonucleases. Alternatively, blunt ends in both the insert and the vector may be ligated. A variety of cloning techniques are disclosed in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989. Such procedures and others are deemed to be within the scope of those skilled in the art.

The vector may be, for example, in the form of a plasmid, a viral particle, or a phage. Other vectors include chromosomal, nonchromosomal and synthetic DNA sequences, derivatives of SV40; bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA, viral DNA such as vaccinia, adenovirus, fowl pox virus, and pseudorabies. A variety of cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, N.Y., (1989).

Particular bacterial vectors which may be used include the commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017), pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden), GEM1 (Promega Biotec, Madison, WI, USA) pQE70, pQE60, pQE-9 (Qiagen), pD10, psiX174 pBluescript II KS, pNH8A, pNH16a, pNH18A, pNH46A (Stratagene), ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia), pKK232-8 and pCM7. Particular eukaryotic vectors include pSV2CAT, pOG44, pXT1, pSG (Stratagene) pSVK3, pBPV, pMSG, and pSVL (Pharmacia). However, any other vector may be used as long as it is replicable and viable in the host cell.

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The host cell may be any of the host cells familiar to those skilled in the art, including prokaryotic cells, eukaryotic cells, mammalian cells, insect cells, or plant cells. As representative examples of appropriate hosts, there may be mentioned: bacterial cells, such as <u>E. coli</u>, <u>Streptomyces</u>, <u>Bacillus subtilis</u>, <u>Salmonella typhimurium</u> and various species within the genera Pseudomonas, Streptomyces, and Staphylococcus, fungal cells, such as yeast, insect cells such as <u>Orosophila S2</u> and <u>Spodoptera Sf9</u>, animal cells such as CHO, COS or Bowes melanoma, and adenoviruses. The selection of an appropriate host is within the abilities of those skilled in the art.

The vector may be introduced into the host cells using any of a variety of techniques, including transformation, transfection, transduction, viral infection, gene guns, or Ti-mediated gene transfer. Particular methods include calcium phosphate transfection, DEAE-Dextran mediated transfection, lipofection, or electroporation (Davis, L., Dibner, M., Battey, I., Basic Methods in Molecular Biology, (1986)).

Where appropriate, the engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes of the present invention. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter may be induced by appropriate means (e.g., temperature shift or chemical induction) and the cells may be cultured for an additional period to allow them to produce the desired polypeptide or fragment thereof.

Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract is retained for further purification. Microbial cells employed for expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents. Such methods are well known to those skilled in the art. The expressed polypeptide or fragment thereof can be recovered and purified from recombinant cell cultures by methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Protein refolding steps can be used, as necessary, in completing configuration of the polypeptide. If desired, high performance liquid chromatography (HPLC) can be employed for final purification steps.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts (described by Gluzman, Cell, 23:175 (1981), and other cell lines capable of expressing proteins from a compatible vector, such as the C127, 3T3, CHO, HeLa and BHK cell lines.

The constructs in host cells can be used in a conventional manner to produce the gene product encoded by the recombinant sequence. Depending upon the host employed in a recombinant production procedure, the polypeptides produced by host cells containing the vector may be glycosylated or may be non-glycosylated. Polypeptides of the invention may or may not also include an initial methionine amino acid residue.

Alternatively, the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof can be synthetically produced

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by conventional peptide synthesizers. In other embodiments, fragments or portions of the polypeptides may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, the fragments may be employed as intermediates for producing the full-length polypeptides.

Cell-free translation systems can also be employed to produce one of the polypeptides of SEO ID Nos: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof using mRNAs transcribed from a DNA construct comprising a promoter operably linked to a nucleic acid encoding the polypeptide or fragment thereof. In some embodiments, the DNA construct may be linearized prior to conducting an *in vitro* transcription reaction. The transcribed mRNA is then incubated with an appropriate cell-free translation extract, such as a rabbit reticulocyte extract, to produce the desired polypeptide or fragment thereof.

The present invention also relates to variants of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. The term "variant" includes derivatives or analogs of these polypeptides. In particular, the variants may differ in amino acid sequence from the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 by one or more substitutions, additions, deletions, fusions and truncations, which may be present in any combination.

The variants may be naturally occurring or created in vitro. In particular, such variants may be created using genetic engineering techniques such as site directed mutagenesis, random chemical mutagenesis, Exonuclease III deletion procedures, and standard cloning techniques. Alternatively, such variants, fragments, analogs, or derivatives may be created using chemical synthesis or modification procedures.

Other methods of making variants are also familiar to those skilled in the art. These include procedures in which nucleic acid sequences obtained from natural isolates are modified to generate nucleic acids which encode polypeptides having characteristics which enhance their value in industrial or laboratory applications. In such procedures, a large number of variant sequences having one or more nucleotide differences with respect to the sequence obtained from the natural isolate are generated and characterized. Preferably, these nucleotide differences result in amino acid changes with respect to the polypeptides encoded by the nucleic acids from the natural isolates.

For example, variants may be created using error prone PCR. In error prone PCR, PCR is performed under conditions where the copying fidelity of the DNA polymerase is low, such that a high rate of point mutations is obtained along the entire length of the PCR product. Error prone PCR is described in Leung, D.W., et al., Technique, 1:11-15 (19 89) and Caldwell, R. C. & Joyce G.F., PCR Methods Applic., 2:28-33 (1992). Briefly, in such procedures, nucleic acids to be mutagenized are mixed with PCR primers, reaction buffer, MgCl₂, MnCl₂, Taq polymerase and an appropriate concentration of dNTPs for achieving a high rate of point mutation along the entire length of the PCR product. For example, the reaction may be performed using 20 fmoles of nucleic acid to be mutagenized, 30pmole of

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each PCR primer, a reaction buffer comprising 50mM KCI, 10mM Tris HCI (pH 8.3) and 0.01% gelatin, 7mM MgCl₂, 0.5mM MnCl₂, 5 units of Taq polymerase, 0.2mM dGTP, 0.2mM dATP, 1mM dCTP, and 1mM dTTP. PCR may be performed for 30 cycles of 94° C for 1 min, 45° C for 1 min, and 72° C for 1 min. However, it will be appreciated that these parameters may be varied as appropriate. The mutagenized nucleic acids are cloned into an appropriate vector and the activities of the polypeptides encoded by the mutagenized nucleic acids is evaluated.

Variants may also be created using oligonucleotide directed mutagenesis to generate site-specific mutations in any cloned DNA segment of interest. Oligonucleotide mutagenesis is described in Reidhaar-Olson, J.F. & Sauer, R.T., et al., Science, 241:53-57 (1988). Briefly, in such procedures a plurality of double stranded oligonucleotides bearing one or more mutations to be introduced into the cloned DNA are synthesized and inserted into the cloned DNA to be mutagenized. Clones containing the mutagenized DNA are recovered and the activities of the polypeptides they encode are assessed.

Another method for generating variants is assembly PCR. Assembly PCR involves the assembly of a PCR product from a mixture of small DNA fragments. A large number of different PCR reactions occur in parallel in the same vial, with the products of one reaction priming the products of another reaction. Assembly PCR is described in U.S. Patent Application Serial No. 08/677,112, filed July 9, 1997 and U.S. Patent Application Serial No. 08/942,504, filed October 31, 1997.

Still another method of genrating variants is sexual PCR mutagenesis. In sexual PCR mutagenesis, forced homologous recombination occurs between DNA molecules of different but highly related DNA sequence in vitro, as a result of random fragmentation of the DNA molecule based on sequence homology, followed by fixation of the crossover by primer extension in a PCR reaction. Sexual PCR mutagenesis is described in Stemmer, W.P., PNAS, USA, 91:10747-10751 (1994). Briefly, in such procedures a plurality of nucleic acids to be recombined are digested with DNAse to generate fragments having an average size of 50-200 nucleotides. Fragments of the desired average size are purified and resuspended in a PCR mixture. PCR is conducted under conditions which facilitate recombination between the nucleic acid fragments. For example, PCR may be performed by resuspending the purified fragments at a concentration of 10-30ng/µl in a solution of 0.2mM of each dNTP, 2.2mM MgCl2, 50mM KCL, 10mM Tris HCl, pH 9.0, and 0.1% Triton X-100. 2.5 units of Taq polymerase per 100µl of reaction mixture is added and PCR is performed using the following regime: 94° C for 60 seconds, 94° C for 30 seconds, 50-55° C for 30 seconds, 72° C for 30 seconds (30-45 times) and 72° C for 5 minutes. However, it will be appreciated that these parameters may be varied as appropriate. In some embodiments, oligonucleotides may be included in the PCR reactions. In other embodiments, the Klenow fragment of DNA polymerase I may be used in a first set of PCR reactions and Tag polymerase may be used in a subsequent set of PCR reactions. Recombinant sequences are isolated and the activities of the polypeptides they encode are assessed.

Variants may also be created by in vivo mutagenesis. In some embodiments, random mutations in a sequence of interest are generated by propagating the sequence of interest in a bacterial strain, such as an E. coli strain, which carries mutations in one or more of the DNA repair pathways. Such "mutator" strains have a higher

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random mutation rate than that of a wild-type parent. Propagating the DNA in one of these strains will eventually generate random mutations within the DNA. Mutator strains suitable for use for in vivo mutagenesis are described in PCT Published Application WO 91/16427.

Variants may also be generated using cassette mutagenesis. In cassette mutagenesis a small region of a double stranded DNA molecule is replaced with a synthetic oligonucleotide "cassette" that differs from the native sequence. The oligonucleotide often contains completely and/or partially randomized native sequence.

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Recursive ensemble mutagenesis may also be used to generate variants. Recursive ensemble mutagenesis is an algorithm for protein engineering (protein mutagenesis) developed to produce diverse populations of phenotypically related mutants whose members differ in amino acid sequence. This method uses a feedback mechanism to control successive rounds of combinatorial cassette mutagenesis. Recursive ensemble mutagenesis is described in Arkin, A.P. and Youvan, D.C., PNAS, USA, 89:7811-7815 (1992).

In some embodiments, variants are created using exponential ensemble mutagenesis. Exponential ensemble mutagenesis is a process for generating combinatorial libraries with a high percentage of unique and functional mutants, wherein small groups of residues are randomized in parallel to identify, at each altered position, amino acids which lead to functional proteins. Exponential ensemble mutagenesis is described in Delegrave, S. and Youvan, D.C., Biotechnology Research, 11:1548-1552 (1993). Random and site-directed mutagenesis are described in Arnold, F.H., Current Opinion in Biotechnology, 4:450-455 (1993).

In some embodiments, the variants are created using shuffling procedures wherein portions of a plurality of nucleic acids which encode distinct polypeptides are fused together to create chimeric nucleic acid sequences which encode chimeric polypeptides. Shuffling procedures are described in U.S. Patent Application Serial No. 08/677,112, filed July 9, 1996, U.S. Patent Application Serial No. 08/942,504, filed October 31, 1997, U.S. Patent No. 5,939,250, issued August 17, 1999, and U.S. Patent Application Serial No. 09/375,605, filed August 17, 1999.

The variants of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 may be (i) variants in which one or more of the amino acid residues of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code.

Conservative substitutions are those that substitute a given amino acid in a polypeptide by another amino acid of like characteristics. Typically seen as conservative substitutions are the following replacements: replacements of an aliphatic amino acid such as Ala, Val, Leu and Ile with another aliphatic amino acid; replacement of a Ser with a Thr or vice versa; replacement of an acidic residue such as Asp and Glu with another acidic residue; replacement of a residue bearing an amide group, such as Asp and Gln, with another residue bearing an amide group; exchange of a basic residue such as Lys and Arg with another basic residue; and replacement of an aromatic residue such as Phe, Tyr with another aromatic residue.

Other variants are those in which one or more of the amino acid residues of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 includes a substituent group.

Still other variants are those in which the polypeptide is associated with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol).

Additional variants are those in which additional amino acids are fused to the polypeptide, such as a leader sequence, a secretory sequence, a proprotein sequence or a sequence which facilitates purification, enrichment, or stabilization of the polypeptide.

In some embodiments, the fragments, derivatives and analogs retain the same biological function or activity as the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80. In other embodiments, the fragment, derivative, or analog includes a proprotein, such that the fragment, derivative, or analog can be activated by cleavage of the proprotein portion to produce an active polypeptide.

Another aspect of the present invention are polypeptides or fragments thereof which have at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or more than 95% homology to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. Homology may be determined using a program, such as FASTA version 3.0t78 with the default parameters, which aligns the polypeptides or fragments being compared and determines the extent of amino acid identity or similarity between them. It will be appreciated that amino acid "homology" includes conservative amino acid substitutions such as those described above.

The polypeptides or fragments having homology to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof may be obtained by isolating the nucleic acids encoding them using the techniques described above.

Alternatively, the homologous polypeptides or fragments may be obtained through biochemical enrichment or purification procedures. The sequence of potentially homologous polypeptides or fragments may be determined by proteolytic digestion, gel electrophoresis and/or microsequencing. The sequence of the prospective homologous polypeptide or fragment can be compared to one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof using a program such as FASTA version 3.0t78 with the default parameters.

The polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5,

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10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof invention may be used in a variety of applications. For example, the polypeptides or fragments thereof may be used to catalyze biochemical reactions. In particular, the polypeptides of SEQ ID NOs: 14 and 46, which have homology to glutamate semialdehyde amino transferase, or fragments thereof, may be used to catalyze the synthesis of 5-aminolevulinate from S-4-amino-5-oxopentanoate. The polypeptides of SEQ ID NOs: 26 and 58, which have homology to triose phosphate isomerase, or fragments thereof, may be used to catalyze the synthesis of glycerone phosphate from D-glyceraldehyde 3-phosphate. The polypeptides of SEQ ID NOs: 32 and 64, which have homology to dCMP dearninase, or fragments thereof, may be used to catalyze the reaction of deoxyctidine and water to produce deoxyuridine and ammonia. The polypeptides of SEQ ID NOs: 38 and 72, which have homology to the MenA protein, or fragments thereof, may be used to catalyze the synthesis of menaquinone. The polypeptide of SEQ ID NO: 80, which has homology to glucose-1-dehydrogenase, may be used to catalyze the synthesis of D-glucono-1,5-lacctone from D-glucose.

The polypeptide of SEQ ID NO: 10, which has homology to lysyl tRNA synthetase, or fragments thereof, may be used to identify compounds capable of specifically inhibiting the growth of *Cenarchaeum symbiosis*, since tRNA synthetases are attractive targets for agents which inhibit growth.

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Agents which specifically inhibit the activity of the lysyl tRNA synthetase from *Cenarchaeum symbiosum* may be identified using a variety of methods known to those skilled in the art. For example, a plurality of agents may be generated using combinatorial chemistry or recombinant DNA libraries encoding a large number of short peptides. The lysyl tRNA synthetases from *Cenarchaeum symbiosum* and control organisms are contacted with the agents and those agents which bind to the lysyl tRNA synthetase from *Cenarchaeum symbiosum* but not to the enzyme from the control organisms are identified. *Cenarchaeum symbiosum* is then contacted with the identified agents to determine which agents inhibit the organism's growth.

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The polypeptides of SEQ ID NOs: 28 and 60, which have homology to the TATA box binding protein, or fragments thereof, may be used to identify promoters in nucleic acids from *Cenarchaeum symbiosis*. In such procedures, the polypeptide or fragment thereof is allowed to contact the nucleic acid and binding of the polypeptide or fragment thereof to the nucleic acid is detected. Binding may be detected by performing a gel shift analysis, a nuclease protection analysis, or by detecting the retention of the nucleic acid on a column matrix having the TATA box binding protein, or a fragment thereof, affixed thereto.

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Compounds which specifically inhibit the binding of the TATA box binding protein of *Generchaeum symbiosis* to promoters may also be used to inhibit growth of the organism. Such compounds may be identified as described above.

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Similarly, agents which specifically inhibit the activity of the polypeptides of SEO ID NOs: 34 and 68, which have homology to RNA helicase, may be used to inhibit the growth of *Cenarchaeum symbiosis*. Such agents may be identified as described above.

The polypeptides of SEO ID NOs: 30 and 62, which have homology to DNA polymerase I, or fragments thereof, may be used to insert a detectable label into a nucleic acid or to generate blunt ends on nucleic acids which have been digested with a restriction endonuclease.

The polypeptides of SEQ ID NOs: 42 and 78, which have homology to site specific DNA methyltranseferases, or fragments thereof, may be used in procedures in which it is desirable to protect nucleic acid sequences from digestion with restriction endonucleases. For example, a nucleic acid sequence having one or more restriction sites therein may be treated with the polypeptides of SEQ ID NOs: 42 or 76 prior to the addition of linkers to the nucleic acid. Thereafter, the linkers may be digested with the restriction enzyme, while the sites in the remainder of the nucleic acid are protected from digestion.

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The polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80, or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof, may also be used to generate antibodies which bind specifically to the polypeptides or fragments. The resulting antibodies may be used to determine whether a biological sample contains *Cenarchaeum symbiosum*. In such procedures, a biological sample is contacted with an antibody capable of specifically binding to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. The ability of the biological sample to bind to the antibody is then determined. For example, binding may be determined by labeling the antibody with a detectable label such as a fluorescent agent, an enzymatic label, or a radioisotope. Alternatively, binding of the antibody to the sample may be detected using a secondary antibody having such a detectable label thereon. A variety of assay protocols which may be used to detect the presence of *Cenarchaeum symbiosum* in a sample are familiar to those skilled in the art. Particular assays include ELISA assays, sandwich assays, radioimmunoassays, and Western Blots.

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Polyclonal antibodies generated against the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof can be obtained by direct injection of the polypeptides into an animal or by administering the polypeptides to an animal, preferably a nonhuman. The antibody so obtained will then bind the polypeptide itself. In this manner, even a sequence encoding only a fragment of the polypeptide can be used to generate antibodies which may bind to the whole native polypeptide. Such antibodies can then be used to isolate the polypeptide from cells expressing that polypeptide.

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For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler and Milstein, 1975, Nature, 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor et al., 1983, Immunology Today 4:72), and the EBV-hybridoma technique (Cole, et al., 1985, in Monoclonal Antibodies and Cancer Therapy, Alan R.

Liss, Inc., pp. 77-96).

Techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778) can be adapted to produce single chain antibodies to the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. Alternatively, transgenic mice may be used to express humanized antibodies to these polypeptides or fragments thereof.

Antibodies generated against the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof may be used in screening for similar polypeptides from other organisms and samples. In such techniques, polypeptides from the organism are contacted with the antibody and those polypeptides which specifically bind the antibody are detected. Any of the procedures described above may be used to detect antibody binding. One such screening assay is described in "Methods for Measuring Cellulase Activities", *Methods in Enzymology*, Vol 160, pp. 87-116.

As used herein the term "nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45,

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57. 59. 61. 63. 65. 67. 71. 75. 79. 3. 7. 11. 15. 17. 19. 21. 23. 35. 39. 43. 47. 49. 51. 53. 55. 69. 73 and 77" encompasses the nucleotide sequences of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, nucleotide sequences homologous to SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or homologous to fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and sequences complementary to all of the preceding sequences. The fragments include portions of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. Preferably, the fragments are novel fragments. Homologous sequences and fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 refer to a sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% or 70% homology to these sequences. Homology may be determined using any of the computer programs and parameters described herein, including BLASTN version 2.0 with the default parameters. Homologous sequences also include RNA sequences in which uridines replace the thymines in the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. The homologous

sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error. It will be appreciated that the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 can be represented in the traditional single character format (See the inside back cover of Stryer, Lubert. *Biochemistry*, 3rd edition. W. H Freeman & Co., New York.) or in any other format which records the identity of the nucleotides in a sequence.

As used herein the term "polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60. 62. 64. 66. 68. 72. 76. 80. 4. 8. 12. 16. 18. 20. 22. 24. 36. 40. 44. 48. 50. 52. 54. 56. 70. 74. and 78" encompasses the polypeptide sequence of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 which are encoded by the extended cDNAs of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, polypeptide seguences homologous to the polypeptides of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78, or fragments of any of the preceding sequences. Homologous polypeptide sequences refer to a polypeptide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% or 70% homology to one of the polypeptide sequences of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Homology may be determined using any of the computer programs and parameters described herein, including FASTA version 3.0t78 with the default parameters or with any modified parameters. The homologous sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error. The polypeptide fragments comprise at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of the polypeptides of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Preferably, the fragments are novel fragments. It will be appreciated that the polypeptide codes of the SEQ ID NDS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 can be represented in the traditional single character format or three letter format (See the inside back cover of Starrier, Lubert. Biochemistry, 3rd edition. W. H Freeman & Co., New York.) or in any other format which relates the identity of the polypeptides in a sequence.

It will be appreciated by those skilled in the art that the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 can be stored, recorded, and manipulated on any medium which can be read and accessed by a computer. As used herein, the words "recorded" and "stored" refer to a process for storing information on a computer medium. A skilled artisan can readily adopt any of the presently known methods for recording information on a computer readable medium to generate manufactures comprising one or more of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37.

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41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, one or more of the polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, 15, or 20 nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

Another aspect of the invention is a computer readable medium having recorded thereon one or more of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, and 79. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, and 79.

Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the nucleic acid codes of SEQ ID NOs. 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 of SEQ ID NOs. 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the the polypeptide codes of SEQ ID NOS. 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, 15, or 20 polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 polypeptide codes of SEO ID NOS. 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Computer readable media include magnetically readable media, optically readable media, electronically readable media and magnetic/optical media. For example, the computer readable media may be a hard disk, a floppy disk, a magnetic tape, CD-ROM, Digital Versatile Disk (DVD), Random Access Memory (RAM), or Read Only Memory (ROM) as well as other types of other media known to those skilled in the art.

Embodiments of the present invention include systems, particularly computer systems which store and manipulate the sequence information described herein. One example of a computer system 100 is illustrated in block diagram form in Figure 3. As used herein, "a computer system" refers to the hardware components, software components,

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and data storage components used to analyze the nucleotide sequences of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the sequences of the polypeptide codes of 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. The computer system 100 preferably includes a processor for processing, accessing and manipulating the sequence data. The processor 105 can be any well-known type of central processing unit, such as the Pentium III from Intel Corporation, or similar processor from Sun, Motorola, Compaq or International Business Machines.

Preferably, the computer system 100 is a general purpose system that comprises the processor 105 and one or more internal data storage components 110 for storing data, and one or more data retrieving devices for retrieving the data storage components. A skilled artisan can readily appreciate that any one of the currently available computer systems are suitable.

In one particular embodiment, the computer system 100 includes a processor 105 connected to a bus which is connected to a main memory 115 (preferably implemented as RAM) and one or more internal data storage devices 110, such as a hard drive and/or other computer readable media having data recorded thereon. In some embodiments, the computer system 100 further includes one or more data retrieving device 118 for reading the data stored on the internal data storage devices 110.

The data retrieving device 118 may represent, for example, a floppy disk drive, a compact disk drive, a magnetic tape drive, etc. In some embodiments, the internal data storage device 110 is a removable computer readable medium such as a floppy disk, a compact disk, a magnetic tape, etc. containing control logic and/or data recorded thereon. The computer system 100 may advantageously include or be programmed by appropriate software for reading the control logic and/or the data from the data storage component once inserted in the data retrieving device.

The computer system 100 includes a display 120 which is used to display output to a computer user. It should also be noted that the computer system 100 can be linked to other computer systems 125a·c in a network or wide area network to provide centralized access to the computer system 100.

Software for accessing and processing the nucleotide sequences of the nucleic acid codes of SEO ID Nos.1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID Nos. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 (such as search tools, compare tools, and modeling tools etc.) may reside in main memory 115 during execution.

In some embodiments, the computer system 100 may further comprise a sequence comparer for comparing the above-described nucleic acid codes of SEO ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 stored on a computer readable medium to reference nucleotide or polypeptide sequences stored on a computer readable medium. A "sequence comparer" refers to one or more programs

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which are implemented on the computer system 100 to compare a nucleotide sequence with other nucleotide sequences and/or compounds stored within the date storage means. For example, the sequence comparer may compare the nucleotide sequences of the nucleic acid codes of SEO ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID Nos. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 78, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 stored on a computer readable medium to reference sequences stored on a computer readable medium to identify homologies or structural motifs. Various sequence comparer programs identified elsewhere in this patent specification are particularly contemplated for use in this aspect of the invention. Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, *Proc. Natl. Acad. Sci. USA 85(8)*:2444-2448; Altschul *et al.*, 1990, *J. Mol. Biol. 215/3)*:403-410; Thompson *et al.*, 1994, *Nucleic Acids Res. 22(2)*:4673-4680; Higgins *et al.*, 1996, *Methods Enzymol. 266*:383-402; Altschul *et al.*, 1990, *J. Mol. Biol. 215/3)*:403-410; Altschul *et al.*, 1999, *J. Mol. Biol. 215/3)*:403-410; Altschul *et al.*, 1993, *Nature Genetics 3*:266-272).

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In one embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well known in the art (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268; Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1993, Nature Genetics 3:266-272; Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402). In particular, five specific BLAST programs are used to perform the following task:

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- BLASTP and BLAST3 compare an amino acid query sequence against a protein sequence database;
- (2) BLASTN compares a nucleotide query sequence against a nucleotide sequence database;
- (3) BLASTX compares the six-frame conceptual translation products of a query nucleotide sequence (both strands) against a protein sequence database;
- (4) TBLASTN compares a query protein sequence against a nucleotide sequence database translated in all six reading frames (both strands); and
- (5) TBLASTX compares the six-frame translations of a nucleotide query sequence against the six-frame translations of a nucleotide sequence database.

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The BLAST programs identify homologous sequences by identifying similar segments, which are referred to herein as "high-scoring segment pairs," between a query amino or nucleic acid sequence and a test sequence which is preferably obtained from a protein or nucleic acid sequence database. High-scoring segment pairs are preferably identified (i.e., aligned) by means of a scoring matrix, many of which are known in the art. Preferably, the scoring matrix used is the BLOSUM62 matrix (Gonnet et al., 1992, Science 256:1443-1445; Henikoff and Henikoff, 1993, Proteins 17:49-61). Less preferably, the PAM or PAM250 matrices may also be used (see, e.g., Schwartz and

Dayhoff, eds., 1978, Matrices for Detecting Distance Relationships: Atlas of Protein Sequence and Structure, Washington: National Biomedical Research Foundation). BLAST programs are accessible through the U.S. National Library of Medicine, e.g., at www.ncbi.nlm.nih.gov.

The BLAST programs evaluate the statistical significance of all high-scoring segment pairs identified, and preferably selects those segments which satisfy a user-specified threshold of significance, such as a user-specified percent homology. Preferably, the statistical significance of a high-scoring segment pair is evaluated using the statistical significance formula of Karlin (see, e.g., Karlin and Altschul, 1990, *Proc. Natl. Acad. Sci. USA 87*:2267-2268).

The parameters used with the above algorithms may be adapted depending on the sequence length and degree of homology studied. In some embodiments, the parameters may be the default parameters used by the algorithms in the absence of instructions from the user.

Figure 4 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database. The database of sequences can be a private database stored within the computer system 100, or a public database such as GENBANK that is available through the Internet.

The process 200 begins at a start state 201 and then moves to a state 202 wherein the new sequence to be compared is stored to a memory in a computer system 100. As discussed above, the memory could be any type of memory, including RAM or an internal storage device.

The process 200 then moves to a state 204 wherein a database of sequences is opened for analysis and comparison. The process 200 then moves to a state 206 wherein the first sequence stored in the database is read into a memory on the computer. A comparison is then performed at a state 210 to determine if the first sequence is the same as the second sequence. It is important to note that this step is not limited to performing an exact comparison between the new sequence and the first sequence in the database. Well-known methods are known to those of skill in the art for comparing two nucleotide or protein sequences, even if they are not identical. For example, gaps can be introduced into one sequence in order to raise the homology level between the two tested sequences. The parameters that control whether gaps or other features are introduced into a sequence during comparison are normally entered by the user of the computer system.

Once a comparison of the two sequences has been performed at the state 210, a determination is made at a decision state 210 whether the two sequences are the same. Of course, the term "same" is not limited to sequences that are absolutely identical. Sequences that are within the homology parameters entered by the user will be marked as "same" in the process 200.

If a determination is made that the two sequences are the same, the process 200 moves to a state 214 wherein the name of the sequence from the database is displayed to the user. This state notifies the user that the sequence with the displayed name fulfills the homology constraints that were entered. Once the name of the stored sequence is displayed to the user, the process 200 moves to a decision state 218 wherein a determination is made whether more sequences exist

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in the database. If no more sequences exist in the database, then the process 200 terminates at an end state 220. However, if more sequences do exist in the database, then the process 200 moves to a state 224 wherein a pointer is moved to the next sequence in the database so that it can be compared to the new sequence. In this manner, the new sequence is aligned and compared with every sequence in the database.

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It should be noted that if a determination had been made at the decision state 212 that the sequences were not homologous, then the process 200 would move immediately to the decision state 218 in order to determine if any other sequences were available in the database for comparison.

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Accordingly, one aspect of the present invention is a computer system comprising a processor, a data storage device having stored thereon a nucleic acid code of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78, a data storage device having retrievably stored thereon reference nucleotide sequences or polypeptide sequences to be compared to the nucleic acid code of SEQ ID Nos.1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 and a sequence comparer for conducting the comparison. The sequence comparer may indicate a homology level between the sequences compared or identify structural motifs in the above described nucleic acid code of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19. 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 or it may identify structural motifs in sequences which are compared to these nucleic acid codes and polypeptide codes. In some embodiments, the data storage device may have stored thereon the sequences of at least 2, 5, 10, 15, 20, 25, 30 or 40 or more of the nucleic acid codes of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NDs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72. 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another aspect of the present invention is a method for determining the level of homology between a nucleic acid code of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 and a reference nucleotide sequence or polypeptide sequence, comprising the steps of reading the nucleic acid code or the polypeptide code and the reference nucleotide or polypeptide sequence through the use of a computer program which determines homology levels and determining homology between the nucleic acid code or polypeptide code and the reference nucleotide or polypeptide sequence with the computer program. The computer program

may be any of a number of computer programs for determining homology levels, including those specifically enumerated herein, including BLAST2N or BLASTN with the default parameters or with any modified parameters. The method may be implemented using the computer systems described above. The method may also be performed by reading at least 2, 5, 10, 15, 20, 25, 30 or 40 or more of the above described nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 through use of the computer program and determining homology between the nucleic acid codes or polypeptide codes and reference nucleotide sequences or polypeptide sequences.

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Figure 5 is a flow diagram illustrating one embodiment of a process 250 in a computer for determining whether two sequences are homologous. The process 250 begins at a start state 252 and then moves to a state 254 wherein a first sequence to be compared is stored to a memory. The second sequence to be compared is then stored to a memory at a state 256. The process 250 then moves to a state 260 wherein the first character in the first sequence is read and then to a state 262 wherein the first character of the second sequence is read. It should be understood that if the sequence is a nucleotide sequence, then the character would normally be either A, T, C, G or U. If the sequence is a protein sequence, then it is preferably in the single letter amino acid code so that the first and sequence sequences can be easily compared.

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A determination is then made at a decision state 264 whether the two characters are the same. If they are the same, then the process 250 moves to a state 268 wherein the next characters in the first and second sequences are read. A determination is then made whether the next characters are the same. If they are, then the process 250 continues this loop until two characters are not the same. If a determination is made that the next two characters are not the same, the process 250 moves to a decision state 274 to determine whether there are any more characters either sequence to read.

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If there aren't any more characters to read, then the process 250 moves to a state 276 wherein the level of homology between the first and second sequences is displayed to the user. The level of homology is determined by calculating the proportion of characters between the sequences that were the same out of the total number of sequences in the first sequence. Thus, if every character in a first 100 nucleotide sequence aligned with a every character in a second sequence, the homology level would be 100%.

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Alternatively, the computer program may be a computer program which compares the nucleotide sequences of the nucleic acid codes of the present invention, to reference nucleotide sequences in order to determine whether the nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 differs from a reference nucleic acid sequence at one or more positions. Optionally such a program records the length and identity of inserted, deleted or substituted nucleotides with respect to the sequence of either the reference polynucleotide or the nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49,

51, 53, 55, 69, 73 and 77. In one embodiment, the computer program may be a program which determines whether the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 contain a single nucleotide polymorphism (SNP) with respect to a reference nucleotide sequence.

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Accordingly, another aspect of the present invention is a method for determining whether a nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 differs at one or more nucleotides from a reference nucleotide sequence comprising the steps of reading the nucleic acid code and the reference nucleotide sequence through use of a computer program which identifies differences between nucleic acid sequences and identifying differences between the nucleic acid code and the reference nucleotide sequence with the computer program. In some embodiments, the computer program is a program which identifies single nucleotide polymorphisms. The method may be implemented by the computer systems described above and the method illustrated in Figure 6. The method may also be performed by reading at least 2, 5, 10, 15, 20, 25, 30, or 40 of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and the reference nucleotide sequences through the use of the computer program and identifying differences between the nucleic acid codes and the reference nucleotide sequences with the computer program.

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In other embodiments the computer based system may further comprise an identifier for identifying features within the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

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An "identifier" refers to one or more programs which identifies certain features within the above-described nucleotide sequences of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. In one embodiment, the identifier may comprise a program which identifies an open reading frame in the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

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Figure 7 is a flow diagram illustrating one embodiment of an identifier process 300 for detecting the presence of a feature in a sequence. The process 300 begins at a start state 302 and then moves to a state 304 wherein a first sequence that is to be checked for features is stored to a memory 115 in the computer system 100. The process 300 then moves to a state 306 wherein a database of sequence features is opened. Such a database would include a list of each feature's attributes along with the name of the feature. For example, a feature name

could be "Initiation Codon" and the attribute would be "ATG". Another example would be the feature name "TAATAA Box" and the feature attribute would be "TAATAA". An example of such a database is produced by the University of Wisconsin Genetics Computer Group (www.gcg.com). Alternatively, the features may be structural polypeptide motifs such as alpha helices, beta sheets, or functional polypeptide motifs such as enzymatic active sites, helix-turn-helix motifs or other motifs known to those skilled in the art.

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Once the database of features is opened at the state 306, the process 300 moves to a state 308 wherein the first feature is read from the database. A comparison of the attribute of the first feature with the first sequence is then made at a state 310. A determination is then made at a decision state 316 whether the attribute of the feature was found in the first sequence. If the attribute was found, then the process 300 moves to a state 318 wherein the name of the found feature is displayed to the user.

The process 300 then moves to a decision state 320 wherein a determination is made whether move features exist in the database. If no more features do exist, then the process 300 terminates at an end state 324. However, if more features do exist in the database, then the process 300 reads the next sequence feature at a state 326 and loops back to the state 310 wherein the attribute of the next feature is compared against the first sequence.

It should be noted, that if the feature attribute is not found in the first sequence at the decision state 316, the process 300 moves directly to the decision state 320 in order to determine if any more features exist in the database.

Accordingly, another aspect of the present invention is a method of identifying a feature within the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising reading the nucleic acid code(s) or polypeptide code(s) through the use of a computer program which identifies features therein and identifying features within the nucleic acid code(s) with the computer program. In one embodiment, computer program comprises a computer program which identifies open reading frames. The method may be performed by reading a single sequence or at least 2, 5, 10, 15, 20, 25, 30, or 40 of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 through the use of the computer program and identifying features within the nucleic acid codes or polypeptide codes with the computer program.

The nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33,

37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 may be stored as text in a word processing file, such as MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE. In addition, many computer programs and databases may be used as sequence comparers, identifiers, or sources of reference nucleotide sequences or polypeptide sequences to be compared to the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. The following list is intended not to limit the invention but to provide guidance to programs and databases which are useful with the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

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The programs and databases which may be used include, but are not limited to: MacPattern (EMBL), DiscoveryBase (Molecular Applications Group), GeneMine (Molecular Applications Group), Look (Molecular Applications Group), MacLook (Molecular Applications Group), BLAST and BLAST2 (NCBI), BLASTN and BLASTX (Altschul et al., *J. Mol. Biol.* 215: 403 (1990)), FASTA (Pearson and Lipman, *Proc. Natl. Acad. Sci. USA*, 85: 2444 (1988)), FASTDB (Brutlag et al. Comp. App. Biosci. 6:237-245, 1990), Catalyst (Molecular Simulations Inc.), Catalyst/SHAPE (Molecular Simulations Inc.), Cerius².DBAccess (Molecular Simulations Inc.), HypoGen (Molecular Simulations Inc.), Insight II, (Molecular Simulations Inc.), Discover (Molecular Simulations Inc.), CHARMm (Molecular Simulations Inc.), Felix (Molecular Simulations Inc.), Modeler (Molecular Simulations Inc.), ISIS (Molecular Simulations Inc.), Quanta/Protein Design (Molecular Simulations Inc.), WebLab (Molecular Simulations Inc.), WebLab Diversity Explorer (Molecular Simulations Inc.), Gene Explorer (Molecular Simulations Inc.), SeqFold (Molecular Simulations Inc.), the MDL Available Chamicals Directory database, the MDL Drug Data Report data base, the Comprehensive Medicinal Chemistry database, Derwents's World Drug Index database, the BioByteMasterFile database, the Genbank database, and the Genseqn database. Many other programs and data bases would be apparent to one of skill in the ert given the present disclosure.

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Motifs which may be detected using the above programs include sequences encoding leucine zippers, helixturn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

The present invention will be further described with reference to the following examples; however, it is to be understood that the present invention is not limited to such examples.

In order to begin the physiological characterization of *Cenarchaeum symbiosum*, it was necessary to obtain enriched preparations of *Cenarchaeum symbiosum* for use in the construction of genomic DNA libraries in fosmid based vectors. Genomic DNA libraries were constructed from two enriched preparations using the methods described in Example 1 below.

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Example 1

Enrichment of Cenarchaeum symbiosum Cells

in Samples Obtained from Axinella Mexicana

Enriched preparations of *Cenarchaeum symbiosum* for use in the preparation of the first fosmid genomic DNA library were obtained essentially as described in Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA **93**, 6241-6246. Briefly, a small individual of *A. mexicana* was incubated in calcium and magnesium-free artificial seawater (ASW) containing 0.25 mg/ml Pronase. The tissue was then homogenized and enriched for archaeal cells by differential centrifugation.

Enriched preparations of *Cenarchaeum symbiosum* for use in preparing the second fosmid genomic DNA library were obtained from a different sponge individual using the following improved enrichment procedure. A small individual of *A. mexicana* was incubated in calcium- and magnesium-free artificial seawater (460mm NaCl, 11mM KCl, 7mM Na₂SO₄, 2mM NaHCO₃) containing 0.25 mg/ml Pronase at room temperature for one hour. The sponge tissue was rinsed in artificial seawater and homogenized in a blender. Large particles and spicules were removed by low-speed centrifugation (4000 rpm, Sorvall GSA rotor at 4°C). The supernatant was next centrifuged at 5000 rpm for 5 min. at 4°C to remove large sponge cells, and the resulting supernatant was centrifuged at 10,000 rpm in a GSA rotor at 4°C for 20 min. to collect the *Cenarchaeum symbiosum* cells. Following centrifugation, the recovered cell fraction containing *Cenarchaeum symbiosum* was further incubated for 1 hr at 4°C in 10 mM Tris/HCl pH 8 and 200 mM EDTA. The cells were then pelleted and subsequently purified on a 15 % Percoll (Sigma) cushion in artificial sea water centrifuged at 2500 rpm in a Beckman SS34 rotor. Archaeal cells banded in the light, upper fraction after centrifugation. This cell fraction was washed in ASW and resuspended in TE buffer (10 mM TrisHCl pH 8, 0.1 mM EDTA). The additional incubation step was found to increase the lysis of sponge cells, which resulted in an enhanced

Quantitative hybridization experiments were performed as described in DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689 using an oligonucleotide specific for archaea having the sequence GTGCTCCCCGCCAATTCCT (SEQ ID NO: 115). These hybridization experiments indicated that 25% to 30% of the total rRNA from this fraction was derived from archaea.

separation of archaeal and eukaryotic cells in the percoll gradient.

The enriched cell preparations were then utilized to construct fosmid libraries as described in Example 2 below.

Example 2

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Construction of Fosmid Libraries

DNA was extracted from the enriched preparations of Example 1 and inserted into fosmids as described in Preston, C. M. et al. 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. Proc. Natl. Acad. Sci. USA 93, 6241-6246 and Stein, J.L. et al. 1996. Characterization of uncultivated prokaryotes: isolation and analysis of a 40-kilobase-pair genome fragment from a planktonic marine archaeon. J. Bacteriol. 178, 591-599. A vertical cross section of sponge (0.5 g) was mechanically dissociated in 0.22 µm filtered, autoclaved seawater using a tissue homogenizer. Cell lysis was accomplished by incubating the dissociated cells in 1 mg of lysozyme per ml for 30 min. at 37°C followed by an incubation for 30 min. at 55°C with 0.5mg of proteinase K per ml and 1% SDS. The tubes were finally placed in a boiling water bath for 60 sec to complete lysis. The protein fraction was removed with two extractions with phenol:chloroform:isoamyl alcohol (50:49:1), pH 8.0, followed by a chloroform: isoamyl alcohol (24:1) extraction. Nucleic acids were ethanol-precipitated and resuspended in TE buffer (10mM Tris.HCI/1mM Na₂-EDTA, pH 8.0). Approximately 5µg of DNA was purified by CsCl equilibrium density gradiant ultracentriguation on a Beckman Optima tabletop ultracentrifuge using a TLA100 rotor. genomic DNA obtained above was inserted into fosmids as follows. The genomic DNA was partially digested with Sau3Al (Promega) and treated with heat-labile phosphatase (HK phosphatase; Epicentre). The partially digested genomic DNA was ligated with pFOS (See U.J. Kim et al., Nucleic Acids Res. 20:1083-1085 (1992)) which had previously been digested with Aatll, phosphatase treated (HK phosphatase), and subsequently digested with BamHl. The ligation mixture was used for in vitro packaging with the Gigapack XL packaging system (Stratagene) selecting for DNA inserts of 35 to 45kb. The phage particles were transfected into E. coli DH10B (Bethesda Research LaboratoriesP and the cells were spread onto LB plates supplemented with 12.5µg/ml chloramphenicol.

Example 3

Identification of Fosmids Containing the Cenarchaeum symbiosum rRNA Operon

The fosmid libraries constructed above were screened to identify clones containing the rRNA operon. PCR reactions were conducted on the library using primers known to amplify the rRNA operon.

The first fosmid library yielded seven unique clones, out of a total of 10,236 recombinant fosmids, which contained the *Cenarchaeum symbiosum* rRNA operon. The second fosmid library yielded eight unique clones, out of a total of 2100 recombinant fosmids, which contained the *Cenarchaeum symbiosum* rRNA operon.

The sequences of the 16S rRNA genes in each of the 15 fosmids containing the *Cenarchaeum symbiosum* rRNA operon were determined. The sequences of the small subunit rRNA genes of these 15 fosmids exhibited variations with respect to one another. Ten of the fosmids contained a small subunit rRNA gene having the sequence of the 16S rRNA gene in the insert of SEQ ID NO: 1, while the remaining fosmids contained a small subunit rRNA gene having the sequence of the 16S rRNA gene in the insert of SEQ ID NO: 2. As discussed in more detail below, the differences in the sequences of the rRNA genes may be used to determine whether a sample contains *Cenarchaeum symbiosum* variant A or *Cenarchaeum symbiosum* variant B.

In addition to determining the sequences of the rRNA genes, the sequences adjacent to the rRNA genes were also determined.

Example 4

Fosmid Sequencing

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Partial restriction enzyme digests were conducted on two purified fosmids, fosmid 101G10 (which contains the variant A sequence) and fosmid 60A5 (which contains the variant B sequence). The partially digested DNA was used to construct plasmid libraries containing inserts of 1-2 kb. The resulting plasmids were sequenced using Applied Biosystems (ABI, Foster City, CA) Prism Dye-terminator FS reaction mix. Direct sequencing from fosmids was used for gap filling and resequencing to ensure accuracy. Fosmid sequencing was performed by using DNA from a single 3 ml overnight culture purified on an Autogen 740 automated plasmid isolation system. Each reaction consisted of one preparation of DNA directly resuspended by the addition of 16 μ l H₂O, 8 μ l oligonucleotide primer (1.4 pmol/ μ l) and 16 μ l ABI Prism Dye-terminator FS reaction mix. Cycle sequencing was performed with a 96° C 3 min. preincubation followed by 25 cycles of the sequence 96° C 20 sec. / 50° C 20 sec. / 60° C 4 min. and a 5 min. post-cycling incubation at 60° C. Sequencing reaction products were analyzed on ABI 377 Prism Sequencers.

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The complete sequences of the *Cenarchaeum symbiosum* derived inserts in the two fosmids are provided in the accompanying sequence listing as SEO ID NO: 1 (fosmid 101G10) and SEO ID NO: 2 (fosmid 60A5). The insert of fosmid 101G10 (SEO ID NO: 1, designated variant A) was 32,998 bp and was syntenic over ca. 28 kbp with the 42,432 bp insert of fosmid 60A5 (SEO ID NO:2, designated variant B). Analysis of the common 28 kbp region is shown in Fig. 1.

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Although the sequences of both fosmids could be aligned unambiguously over most of the overlapping region, four large insertion/deletions ranging in size from 142 bp to 1994 bp were identified between positions 20,500 and 25,800. The longest insertion contained a repetitive element of 1784 bp, that was found in the sequence of SEQ ID NO: 1 between *men*A and ORFO5. It was composed of a 3-fold direct repeat of 575 bp (rep1 through 3 in Fig. 1), with repeats exhibiting only minor sequence variation (95.8% to 98.7% identity).

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A segment of 56 bp at the start of this repeat was also found adjacent to the 3' terminus of the third direct repeat. No obvious structural or sequence similarities to known repeats or mobile genetic elements from other organisms were identified within the repeat sequence. Its occurrence in only one variant and its relatively low G+C content relative to the rest of the fragment suggest that it may have been acquired by horizontal transfer from a different genetic context.

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The sequenced regions contained several open reading frames or RNA encoding sequences. Some of the identified open reading frames encode proteins having homology to previously identified proteins. In particular, some of the open reading frames encode proteins involved in several metabolic pathways, providing insight into the physiology of *Cenarchaeum symbiosum*.

An open reading frame which encodes a protein having homology to glutamate semialdehyde aminotransferase (a protein involved in heme biosynthesis) was identified between nucleotides 7604-8908 of the

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insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 23558-24682 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 45 and 13 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 46 and 14 respectively in the accompanying sequence listing. A gene encoding glutamate semialdehyde aminotransferase has also been detected in a rRNA operon containing genomic fragment of a planktonic marine crenarchaeote. (Stein, J.L. et al. 1996. Characterization of uncultivated prokaryotes: isolation and analysis of a 40-kilobase-pair genome fragment from a planktonic marine archaeon. J. Bacteriol. 178, 591-599)

An open reading frame encoding a protein having homology to triose-phosphate isomerase was identified between 13944-14612 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 29655-30491 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 57 and 25 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 58 and 26 respectively in the accompanying sequence listing. This triosephosphate isomerase represents the first such protein sequence reported in a crenarchaeote, and shares known archaeal signature sequences and deletions which distinguish archaeal triosephosphate isomerase genes from their eucaryal and eubacterial homologues.

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An open reading frame encoding a protein having homology to the TATA binding protein was identified between 14616-15164 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 30501-31049 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 59 and 27 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 60 and 28 respectively in the companying sequence listing. This TATA box-binding protein (TBP) is similar to other known archaeal TBP's and is N-terminally truncated with respect to the eukaryal homologs. It shares 49% amino acid similarity with TBP from *Pyrococcus woesii*.

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An open reading frame encoding a protein having homology to DNA polymerase (a protein involved in DNA replication and repair) was identified between nucleotides 15488-18025 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 31371-33905 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 61 and 29 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 62 and 30 respectively in the accompanying sequence listing.

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The DNA polymerase of *Cenarchaeum symbiosum* has a high degree of similarity to the crenarchaeal homologs from the extreme thermophiles *Sulfolobus acidocaldarius* and *Pyrodictium occultum* (54% and 53% resp.) and exhibits all conserved motifs of B-(a-)type DNA polymerases and 3'-5'-exonuclease motifs, both indicative of archaeal polymerases. A more detailed phylogenetic analysis and biochemical characterization of the *C. symbiosum* polymerase has been published elsewhere. (Schleper, C., *et al.* 1997. Characterization of a DNA polymerase from the uncultivated psychrophilic archaeon *Cenarchaeum symbiosum*. *J. Bact.* 179, 7803-7811)

An open reading frame which encodes a protein having homology to dCMP deaminase (a protein involved in pyrimidine synthesis) was identified between nucleotides 18022-18663 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 33902-34456 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 63 and 31 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 64 and 32 respectively in the accompanying sequence listing.

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An open reading frame encoding a protein having homology to the ATP dependent RNA helicase (a protein involved in translation) was identified between nucleotides 18638-20149 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 34559-36067 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 65 and 33 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 66 and 34 respectively in the accompanying sequence listing. The identified ATP RNA helicase is highly similar in sequence to homologues found in the genomic sequences of three euryarchaeota (Bult, C., et al. Complete genome sequence of the methanogenic archaeon, Methanococcus jannaschii. Science 273, 1058-1073; Klenk, H.P. et al. 1997. The complete genome sequence of the hyperthermophilic, sulphate-reducing archaeon Archaeoglobus fulgidus. Nature 390, 364-370; Smith, D. R.et al. 1997. Complete genome sequence of Methanobacterium thermoautotrophicum delta H: functional analysis and comparative genomics. J. Bacteriol. 179, 7135-7155).

An open reading frame encoding a protein having homology to MenA (a protein involved in menaquinone biosynthesis) was identified between nucleotides 20956-21834 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 37404-38282 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 71 and 37 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 72 and 38 respectively in the accompanying sequence listing.

An open reading frame encoding a protein having homology to the site specific DNA methyltranseferase proteins involved in restriction/modification was identified between nucleotides 26378-27454 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 40563-41669 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 75 and 41 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 76 and 42 respectively in the accompanying sequence listing.

An open reading frame encoding a protein having homology to the histone H1 DNA binding protein was identified between nucleotides 10625-1134 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 5 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 6 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to lysyl tRNA synthetase was identified between nucleotides 13046-14620 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned

SEQ ID No: 9 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 10 in the accompanying sequence listing.

A hypothetical open reading frame was identified between nucleotides 11478-13046 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 7 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 8 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to peptidylprolyl cis/trans isomerase (a chaperone) was identified between nucleotides 20156-20434 of the insert from fosmid 101G10 (SEQ ID NO: 1) on the strand complementary to that provided in the sequence listing. This open reading frame has been assigned SEQ ID No: 67 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 68 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to glucose-1-dehydrogenase was identified between nucleotides 28065-29843 of the insert from fosmid 101G10 (SEQ ID NO: 1). This open reading frame has been assigned SEQ ID No: 79 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 80 in the accompanying sequence listing.

A hypothetical open reading frame designated Hypothetical O1 was identified between nucleotides 1358-2290 of the insert from fosmid 101G10 (SEO ID NO: 1) and between nucleotides 17329-18213 of the insert from fosmid 60A5 (SEO ID NO: 2) on the strands complementary to the insert strands provided in SEO ID NOs: 1 and 2. These open reading frames have been assigned SEO ID NOs: 43 and 11 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEO ID NOs: 44 and 12 respectively in the accompanying sequence listing.

A hypothetical open reading frame designated Hypothetical O2 was identified between nucleotides 8961-9767 of the insert from fosmid 101G10 (SEO ID NO: 1) between nucleotides 24913-25728 of the insert from fosmid 60A5 (SEO ID NO: 2). These open reading frames have been assigned SEO ID NOs: 47 and 15 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEO ID NOs: 48 and 16 respectively in the accompanying sequence listing.

An open reading frame designated ORF 01 was identified between nucleotides 9772-10479 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 25732-26427 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 49 and 17 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 50 and 18 respectively in the accompanying sequence listing.

An open reading frame designated ORF 02 was identified between nucleotides 10545-10922 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 26504-26881 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 51 and 19 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 52 and 20 respectively in the accompanying sequence listing.

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An open reading frame designated ORF 03 was identified between nucleotides 11382-11987 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 27337-27936 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 53 and 21 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 54 and 22 respectively in the accompanying sequence listing.

An open reading frame designated ORF 04 was identified between nucleotides 12916-13737 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 28822-29631 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 55 and 23 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 56 and 24 respectively in the accompanying sequence listing.

An open reading frame designated Hypothetical O3 was identified between nucleotides 20554-20955 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 37002-37403 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 69 and 35 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 70 and 36 respectively in the accompanying sequence listing.

An open reading frame designated ORF 05 was identified between nucleotides 25151-26377 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 39454-40572 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 73 and 39 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 74 and 40 respectively in the accompanying sequence listing.

An open reading frame encoding a protein with no homology to known proteins was identified between nucleotides 3-10421 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 3 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 4 in the accompanying sequence listing.

An open reading frame designated ORFO6 was identified between nucleotides 27535-28002 of the insert from fosmid 101G10 (SEQ ID ND: 1). This open reading frame has been assigned SEQ ID No: 77 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 78 in the accompanying sequence listing.

A gene coding for tRNA^{Tyr} was identified between nucleotides 12129-12251 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 28058-28180 of the insert from fosmid 60A5 (SEQ ID NO:2). This tRNA contains a 45 bp intron in the vicinity of the anticodon loop.

Table 1 shows the level of homology between the open reading frames in the inserts from fosmid 101G10 and fosmid 60A5 at the nucleic acid level. Table 1 also shows the level of homology at the amino acid level between

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the polypeptides encoded by the insert from fosmid 101G10 and fosmid 60A5. Nucleic acid homology was calculated using BLASTN with the default parameters. Amino acid homology was calculated using FASTA with the parameters. As shown in Table 1 and Fig. 1, the protein coding regions were highly similar in both nucleic acid and deduced amino acid sequences.

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Over the 28 kb common region in the 101610 and 60A5 inserts, the inserts shared > 99.2% identity in their ribosomal RNA genes, approximately 87.8% overall DNA identity, an average of 91.6% similarity in ORF amino acid sequence, and complete colinearity of protein encoding regions. As shown in Table 1, in protein coding regions the DNA identity of the two contigs ranged from 80.9% (triose phosphate isomerase) to 91.5% (Hypothetical 03). Within intergenic regions the identity dropped to 70 - 86 %, and small insertions or deletions were found frequently. The high similarity in coding regions and upstream sequences aided in the identification of genes, start codons, and putative transcriptional promoter motifs (see below). Genes appear as densely packed in *C. symbiosum* as they are in other sequenced archaeal genomes (Bult, C., et al. 1996. Complete genome sequence of the methanogenic archaeon, *Methanococcus jannaschii. Science* 273, 1058-1073, Klenk, H.P. et al. 1997. The complete genome sequence of the hyperthermophilic, sulphate-reducing archaeon *Archaeoglobus fulgidus*. *Nature* 390, 364-370; Smith, D. R., et al. 1997. Complete genome sequence of *Methanobacterium thermoautotrophicum* delta H: functional analysis and comparative genomics. *J. Bacteriol.* 179, 7135-7155).

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The ribosomal RNA operon of *Cenarchaeum symbiosum* is composed of the genes for the 16S and 23S rRNAs separated by a spacer of 131 bp. This organization is typical of crenarchaeotes, and differs from rRNA operons of euryarchaeotes, which usually contain 5S RNA and tRNA genes. (Garrett, R. A. *et al.* 1991. Archaeal rRNA operons. *TIBS* 16, 22-26). The large subunit rRNA genes are located between nucleotides 2680-5674 of SEQ ID NO: 1 (fosmid 101G10) and between nucleotides 18645-21639 of SEQ ID NO: 2 (fosmid 60A5). The small subunit rRNA genes are located between nucleotides 5806-7278 of SEQ ID NO: 1 (on the opposite strand from that shown in the Sequence Listing, as indicated in Figure 1) and between nucleotides 21771-23243 of SEQ ID NO: 2. The large and small subunit rRNA genes in the two fosmids were 99.2% and 99.3% identical, respectively.

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As mentioned above, the sequences of the *Cenarchaeum symbiosum* derived inserts in fosmids 101610 and 60A5 had a high degree of homology but were not completely identical. The sequence of the insert in fosmid 101G10 was designated variant A, while the sequence of the insert in fosmid 60A5 was designated variant B. Such sequence differences could arise if the fosmid inserts were derived from two closely related but distinct strains of *Cenarchaeum symbiosum* or, alternatively, the sequence differences could be due to cloning or sequencing artifacts. To confirm that the fosmid inserts were in fact derived from two closely related strains, portions of the inserts in a plurality of different fosmids were sequenced to determine whether they were identical to either of the inserts in fosmids 101G10 and 60A5, as would be the case if there were in fact two closely related strains of *Cenarchaeum symbiosum*.

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In particular, the ribosomal RNA spacer regions of variant A and variant B contained 10 distinguishing signature nucleotides and the 16S rRNA genes of variant A and variant B contained two distinguishing nucleotides.

Example 5 provides the results of a PCR based analysis of the 16S rRNA gene and the 16S-23S spacer region in 13 different fosmid inserts.

Example 5

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PCR Based Analysis of Fosmid Inserts to Determine

Whether they Contain the Variant A or Variant B Sequences

Primers 21F and 459R-LSU (CTTTCCCTCACGGTA, SEQ ID NO: 116) were used to amplify the 16S-23S spacer region from the fosmids. The amplification products were sequenced using primer SP23rev (CTA TTG CCG TCT TTA CACC, SEQ ID NO: 117).

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PCR reactions with two archaea-specific 16S rDNA primers (21F and 958R (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689), one of which was biotinylated, were used to amplify a 950 base pair (bp) fragment from the fosmids. The PCR products were purified and sequenced as described in Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6246 with primer 519R 16S rDNA

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The results of this analysis are shown in Table 2. As shown in Table 2, in samples obtained from several unique rRNA operon-containing fosmids, a sequence identical to either variant A (101G10) or variant B (60A5) was present.

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The above methods may also be used to determine whether a biological sample contains variant A and/or variant B. In such procedures, nucleic acids are obtained from the biological sample, amplified using the above primers, and sequenced using the above oligonucleotide to determine whether the sample contains the variant A and/or the variant B sequence.

Similarly, the amplification reaction may be conducted using any primers which generate amplification products having sequences which differ between variant A and variant B. The amplification products may then be sequenced to determine whether they have the sequence of variant A and/or variant B. In some embodiment, the amplification reaction may be conducted under conditions in which the amplification primers specifically hybridize to one of the variants.

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RFLP analyses were also be used to assess whether the fosmids contained the sequence of variant A or variant B as described in Exemple 6 below.

Example 6

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RFLP Based Analysis of Fosmids to Determine Whether

They Contain the Variant A or Variant B Sequences

Primer set 21F (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689) and 459R-LSU for the amplification of 2.2 kbp of the ribosomal operon, primer set GSAT810F (GAATCCGCC CCCGACTATCTT, SEQ ID NO: 118) and 16S37REV (CATGGCTTAGTATCAATC SEQ ID NO: 119) for the amplification of the 16S RNA-GSAT region (2.2 kbp) and primer set Cenpol357F (ACITACAACGGI GACGAYTTTGA

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SEQ ID NO: 120) and Cenpol735R (CACCCCGAARTAGTTYTTYTT SEQ ID NO: 121) for an internal DNA polymerase fragment (of 1134 bp) were used in PCR reactions with 5 ng of purified fosmids. The PCR products were cut with Taql and Hpall (16S-23S RNA), HaellI and Rsal (GSAT-16S RNA) or HaellI and Avail (polymerase) and analyzed on 2 % agarose gels.

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The results are shown in Table 2. If the pattern did not exactly match but closely resembled the RFLP of either type A or B, it was assigned as a lower case letter (a or b, Table 2), meaning that at least 3 out of 4 or 3 out of 5 bands created by restriction digest appear identical in size to the ones from either type A or B. As shown in Table 2, RFLP patterns of the 1150 bp fragment covering the 5'-end of the GSAT gene and 16S gene and the internal fragment of 1134 bp from the DNA polymerase gene revealed that all fosmids analyzed could again be assigned to either the A or B type, although slight variations were also detected (lower case letters in Table 2), suggesting that both variants exhibit further microheterogeneity which is detectable in protein coding and intergenic regions.

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The above methods may also be used to determine whether a biological sample contains variant A and/or variant B. In such procedures, nucleic acids are obtained from the biological sample, amplified using the above primers, and digested as described above to determine whether the sample contains the variant A and/or the variant B sequence. Similar analyses may also be performed using other portions of the sequences of SEQ ID NOs: 1 and 2 which are different from one another.

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To further confirm the existence of two closely related strains of *Cenarchaeum symbiosum*, biological samples were obtained from several individual sponges and analyzed to determine whether the samples contained variant A and/or variant B. Example 7 below provides the results of a PCR analysis of the *Cenarchaeum symbiosum* 16S rRNA genes in samples obtained from several individual sponges in different locations and at different times.

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Example 7

Analysis of Samples from Individual Sponges

The 16S rRNA genes of variant A and variant B differ at positions 175 and 183.7 (E. coli numbering). PCR

reactions with two archaea-specific 16S rDNA primers (21F and 958R (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689), one of which was biotinylated, were used to amplify a 950 base pair (bp) fragment from total nucleic acids derived from several different sponge individuals. The PCR products were purified and sequenced as described in Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6248 with primer

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519R.

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The amplification products were sequenced to determine whether they corresponded to variant A and/or variant B. The results are shown in Table 3. As shown in Table 3, in 15 out of 16 cases U/C ambiguities were found at the signature positions, indicating the presence of both variants in samples obtained from a single sponge (Table 3). Only one sponge (S4) yielded an unambiguous sequence identical to variant A, but variant B was detected in this individual by another criterion (see below).

Hybridization analyses were also used to determine whether individual sponges harbored variant A and/or variant B. The results of these analyses are provided in Example 8 below.

Example 8

<u>Hybridization Based Analysis of Samples Obtained from Axinella Mexicana</u> to Determine Whether the Samples Contain Variant A and/or Variant B

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Two oligonucleotides specific for each variant type were designed from the 23S rDNA gene sequences of fosmids 101G10 and 60A5. The probes differed in 3 positions and have the sequences ACACTTCAACTATTTCCTG (SEQ ID NO: 122 variant A) and ACACTTTGACTATTTCGTG (SEQ ID NO: 123, variant B). Nucleic acid samples from individual sponges (300 ng) and controls (fosmids 101G10 and 60A5, 50 ng each) were denatured, bound to nylon membranes (Hybond-N, Amersham), hybridized with the labeled probes (Massana, R. et al. 1997. Vertical distribution and phylogenetic characterization of marine planktonic Archaea in the Santa Barbara Channel. *Appl. Env. Microb.* 63, 50-56) and washed at 41.5 °C. Hybridization was analyzed by autoradiography.

The results are provided in Table 3. In the samples from the majority of host sponges examined, the presence of both 23S rRNA variants was observed, confirming that the specific association of *C. symbiosum* with its host typically involves the presence of both variants.

The data provide strong evidence that these genomic clones are derived from two very closely related, but distinct strains, as opposed to representing two ribosomal RNA operon regions originating from the same organism. This conclusion is consistent with the observation that all crenarchaeota characterized to date contain only one ribosomal RNA operon (Garrett, R. A. et al. 1991. Archaeal rRNA operons. *TIBS* 16, 22-26).

The high conservation between the inserts in fosmid 101G10 and fosmid 60A5 was not entirely confined to coding regions but also extended into adjacent upstream sequences. Due to this upstream similarity, and also because the average G+C content of the sequences was relatively high, it was possible to readily identify prospective transcriptional (A+T rich) promoter elements. A motif corresponding to the consensus of the archaeal TATA-box-like element (C/T-T-A-T/A-A) (Hain, J. et al. 1992. Elements of an archaeal promoter defined by mutational analysis. *Nucl. Acids. Res.* 20, 5423-5428) was identified upstream of nearly all genes (Fig. 2). The exceptions were the genes encoding MenA and DNA polymerase which are located immediately downstream of other ORFs and may therefore be transcribed as polycistronic mRNAs. *In vivo* and *in vitro* studies in other archaea have shown that initiation of transcription occurs consistently 24 to 28 bp downstream from the central T of this motif (Hain, J et al. 1992. Elements of an archaeal promoter defined by mutational analysis. *Nucl. Acids. Res.* 20, 5423-5428; Palmer, J. R. and Daniels, C.J. 1995. In vivo definition of an archaeal promoter. *J. Bacteriol.* 177 1844-1849). For twelve of the protein encoding genes, the promoter element was found 25 to 30 bp upstream of the ORF (Fig. 2), suggesting that transcriptional initiation occurs in close proximity to, or directly at, the translational start codon.

A similar observation has been made for 30 of the predicted 100 strong and medium promoters from 156 kbp sequence of Sulfolobus solfataricus (Sensen, C. W. et al. 1996. Organizational characteristics and information

content of an archaeal genome: 156 kb of sequence from Sulfolobus solfataricus P2. Molec. Microb. 22, 175-191). Transcription initiation at, or in clòse proximity to, the translational start codons has been mapped for some genes in Halobacterium salinarium (Brown, J.W. et al. 1989. Gene structure, organization, and expression in archaebacteria. CRC Crit. Rev. Microb. 16, 287-337) and S. solfataricus (Klenk, H.P., et al. 1993. Nucleotide sequence, transcription and phylogeny of the gene encoding the superoxide dismutase of Sulfolobus acidocaldarius. Biochim. Biophys. Acta 1174 95-98), and alternative mechanisms for initial mRNA-ribosome contact in Archaea have been hypothesized (Brown, J.W. et al. 1989. Gene structure, organization, and expression in archaebacteria. CRC Crit. Rev. Microb. 16, 287-337).

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The promoters listed in Figure 2, or fragments thereof, may be used in expression vectors or expression systems. In one embodiment, the promoters listed in Figure 2 may be operably linked to coding regions and introduced into archaebacteria, and in particular *Cenarchaeum symbiosum*, to express the encoded gene product in the archaebacterial cells.

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Alternatively, the promoters listed in Figure 2 may be operably linked to coding regions and introduced into host cells which are not normally capable of directing transcription from archaebacterial promoters. In addition, genes encoding the proteins required for transcription from these promoters are also introduced into the host cells. The genes encoding these transcription factors may be on the same vector as the promoter from *Cenarchaeum symbiosum* or on a different vector. In some embodiments, the genes encoding these transcription factors are linked to an inducible promoter. Expression of the transcription factors is induced when it is desired to express the proteins which are operably linked to the promoter from *Cenarchaeum symbiosum*.

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Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims.

Table 1

Comparison of Overlapping Coding Sequences from Fosmid 101G10 and Fosmid 60A5

| Gene | Functional | | entity |
|--------------------|--------------------------|------------|------------|
| Name ¹ | Category | Nucleotide | Amino Acid |
| Hypothetical 01 | unknown | 81.4 | 76.6 |
| 23\$ | translation | 99.16 | |
| 168 | translation | 99.3 | |
| GSAT | heme biosynthesis | 83.2 | 83.8 |
| Hypothetical 02 | unknown | 83.4 | 81.4 |
| ORF 01 | unknown | 83.3 | 85.7 |
| ORF 02 | unknown | 89.9 | 95.2 |
| ORF 03 | unknown | 87.9 | 86.7 |
| tRNA ^{ny} | translation | 99.2 | |
| ORF 04 | unknown | 87.8 | 88.1 |
| TIM | glycolysis | 80.9 | 83.3 |
| TBP | transcription | 83.4 | 86.3 |
| DNA polymerase | replication/repair | 89.0 | 93.9 |
| dCMP deaminase | pyrimidine synthesis | 85.7 | 89.8 |
| RNA helicase (ATP | translation | 86.1 | 92.2 |
| dependent) | | | |
| PPI | chaperone | 88.4 | 92.5 |
| Hypothetical 03 | unknown | 91.5 | 92.4 |
| MenA | menaquinone biosynthesis | 86 | 89.4 |
| ORF 05 | unknown | 87.5 | 90.6 |
| Methylase | restriction/modification | 86.4 | 87.5 |

¹ Hypothetical: open reading frame (ORF) with similarity to proteins of unknown function from the databases.

ORF = open reading frame identified by similarity between both fosmids, including upstream promoter sequence;

GSAT = glutamate semialdehyde aminotransferase; TIM = triose-phosphate isomerase; TBP = TATA box-binding protein; PPI = peptidylprolyl cis/trans isomerase.

Table 2

Analysis of Polymorphism at Four Distinct Loci in Different Fosmids

| Fosmid | 16S RNA" | 16S-23S | 16S-GSAT*3 | | DNA Pol ^{*3} | |
|--------|----------|----------|------------|------|-----------------------|-------|
| | | spacer*2 | Haelli | Rsal | HaellI | Avall |
| 101G10 | A | Α | A, | Α | A | Α |
| 60A5 | В | В | В | B | В | В |
| 15A5 | В | В | •• | •• | b | b |
| 43H4 | A | | •• | •• | A | A |
| 60H6 | A | A | •• | •• | a/b | В |
| 69H2 | A | •• | •• | •• | A | A |
| 87F4 | В | | •• | •• | b | a/b |
| C1H5 | A | Α | . А | Α | | |
| C4H1 | A | Α | Α | Α | | |
| C4H9 | Α | A | A | Α | A | В |
| C7D4 | Α | Α | Α | Α | Α | Α |
| C8B8 | В | В | В | В | В | b |
| C15A3 | A | A | Α | Α | | |
| C17D2 | В | •• | b | В | В | b |
| C20B5 | A | Α | a | a/b | | |

^{*1:} partial sequence (101G10 through 87F4) or RFLP analysis (C1H5 through C20B5).

The first seven fosmids were isolated from a first library, the last 8 fosmids (prefix C) are from a second library.

^{*2:} partial sequence.

^{*3:} RFLP analysis of PCR products; A/B: identical pattern to either 101G10 (-A) or 60A5 (-B); a,b: similar pattern to either A or B (see materials and methods). Fosmids C1H5, C4H1, C15A3 and C20B5 did not yield PCR products with polymerase-specific primers.

 $[\]cdot \cdot =$ not determined.

Table 3

Detection of *C. symbiosium* Variants in Natural Populations of *A. mexicana*

| A. mexicana Individual or Isolated DNA Source* | Variation in 16S rDNA Positions** | | Variations in 23S rRNA
Hybridization | | |
|--|-----------------------------------|-------|---|----------------|--|
| 10010100 DITA OOUIDO | 175 | 183.7 | Variant Type A | Variant Type E | |
| fosmid 101G10 from s12 | U | IJ | + | | |
| fosmid 60A5 from s12 | C | С | | + | |
| s12 | Y | Y | + | + | |
| s1 | | ••• | + | + | |
| s 2 | *** | ••• | + | + | |
| s3 | Y | Y | + | + | |
| 34 | U | U | + | w | |
| s 5 | Y | . ү | *** | ••• | |
| s6 | Y | Y | + | + | |
| s7 | ••• | ••• | + | w | |
| s8 | Y | Y | + | + | |
| s 9 | Y | Y | + | w | |
| s10 | ••• | ••• | + | + | |
| s 11 | Y | Y | + | + | |
| s13 | *** | ••• | + | + | |
| s14 | ••• | ••• | + | w | |
| s16 | ••• | ••• | + | + | |
| s17 | ••• | ••• | • | w | |
| s18 | Y | Y | - | w | |
| s19 | ••• | ••• | + | + | |
| s20 | | ••• | + | + | |
| s21 | ••• | *** | + | + | |
| s 22 | ••• | *** | + | + | |
| s23 | *** | ••• | + | + | |
| s24 | ••• | • | + | + | |
| s 25 | | | + | + | |
| s26 | ••• | ••• | + | + | |
| s27 | ••• | ••• | + | + | |
| s28 | ••• | ••• | + | + | |
| s28 | ••• | *** | + | + | |
| s 30 | ••• | *** | + | + | |
| hs1 | ••• | *** | + | + | |
| hs2 | ••• | *** | + | + | |
| hs3 | Y | Y | + | w | |
| hs4 | Y | Y | + | w | |
| hs5 | Y | Y | + | + | |
| hh1 | ••• | *** | w | w | |
| hh2 | Y | Y | + | + | |
| hh3 | Ý | Y | + | + | |
| Aq1 | Ÿ | Y | | | |
| Aq2 | Ý | Y | *** | ••• | |
| Aq3 | • | ••• | + | + | |

^{*}s = Naples Reef; hs = Haskle; hh = Hermit Hole; Aq = captive sponge.

^{**}Y = direct sequence of PCR product yields C and U at the same position.

^{··· =} not determined; w = weakly positive.

WHAT IS CLAIMED IS:

1. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2, the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2, fragments comprising at least 10 consecutive nucleotides of SEQ ID NO: 1 and SEQ ID NO: 2, and fragments comprising at least 10 consecutive nucleotides of the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2.

- 2. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of high stringency.
- An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of moderate stringency.
- 4. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of low stringency.
- 5. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 1 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 6. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 1 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 7. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEO ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto.
- 8. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of high stringency.
- An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of moderate stringency.
- 10. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of low stringency.
- 11. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 7 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 12. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 7 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 13. An isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto.
- 14. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 13 as determined by analysis with BLASTN version 2.0 with the default parameters.

15. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto.

- 16. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of high stringency.
- 17. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of moderate stringency.
- 18. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of low stringency.
- 19. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 15 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 20. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 15 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 21. An isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto.
- 22. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 21 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 23. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 21 as determined by analysis with BLASTN version 2.0 with the default parameters.
- An isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- 25. An isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- An isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- An isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- 28. An isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

29. An isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of Claim 28.

- 30. An isolated or purified polypeptide having at least 70% homology to the polypeptide of Claim 28 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 31. An isolated or purified polypeptide having at least 99% homology to the polypeptide of Claim 28 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 32. An isolated or purified polypeptide having at least 70% homology to the polypeptide of Claim 29 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 33. An isolated or purified polypeptide having at least 99% homology to the polypeptide of Claim 29 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 34. An isolated or purified polypeptide comprising a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- 35. An isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of Claim 34.
- 36. An isolated or purified polypeptide having at least 70% homology to the polypeptides of Claim 34 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 37. An isolated or purified polypeptide having at least 99% homology to the polypeptides of Claim 34 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 38. An isolated or purified polypeptide having at least 70% homology to the polypeptides of Claim 35 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 39. An isolated or purified polypeptide having at least 99% homology to the polypeptides of Claim 35 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 40. An isolated or purified antibody capable of specifically binding to a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- An isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- 42. An isolated or purified antibody capable of specifically binding to a polypeptide having a sequence selected from the group consisting of SEQ ID NDs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- An isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

A method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

- 45. A method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
- 46. A method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
- 47. A method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
 - 48. A method of generating a variant comprising:

obtaining a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, the sequences complementary to the sequences of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments comprising at least 30 consecutive nucleotides of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEQ ID NOS. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77; and

changing one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence.

- 49. The method of Claim 48, further comprising the step of testing the enzymatic properties of a translation product of said variant.
- A computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- A computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEOID NOs. 1, 2, 5, 9, 13, 25,

27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

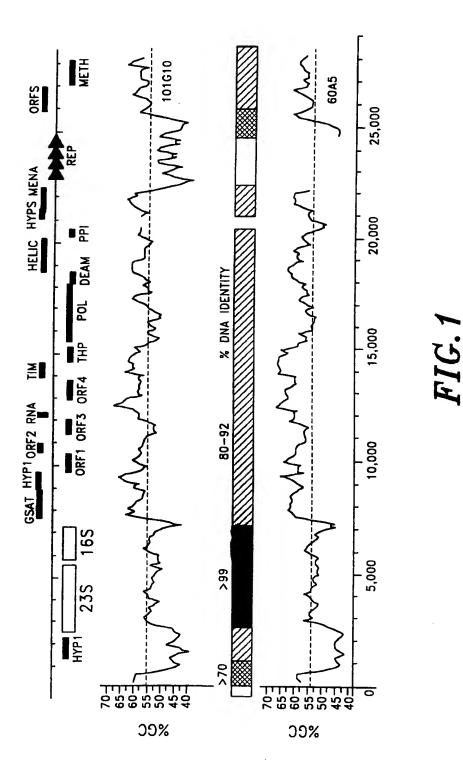
- The computer system of Claim 51 further comprising a sequence comparer and a data storage device having reference sequences stored thereon.
- The computer system of Claim 52 wherein said sequence comparer comprises a computer program which indicates polymorphisms.
- The computer system of Claim 51 further comprising an identifier which identifies features in said sequence.
- A method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of:

reading said first sequence and said reference sequence through use of a computer program which compares sequences; and

determining differences between said first sequence and said reference sequence with said computer program.

- The method of Claim 55, wherein said step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.
- A method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of:

reading said sequence through the use of a computer program which identifies features in sequences; and identifying features in said sequence with said computer program.



SUBSTITUTE SHEET (RULE 26)

| Seq.
ID No. | Gene | Strain | TATA Box | Coding Start | TATA to Start (b) |
|----------------|------------|--------------|------------------------|-----------------------|---|
| ;;† ¢ | Hypoth 03 | A AAGCTAGACT | TGGG | GCGCCCATG | 25 |
| 7 R | | AAG | TGGG | CCGCCCTC | 1 |
| 83 | Hypoth 02 | GGA | 9990 | CGGGGCCCAT G | |
| 84 | | | ATTATA CGGG CGTACATTCC | CGGGGCCCAT G | 1 1 4 5 1 1 4 6 1 |
| 82 | ORF C2 | AAG | _ | AACGGCCGTA TG | 27 |
| 986 | | | AATAAT AGCC TGCCGTCCGT | ACCIGCGIA IG | |
| 87 | ORF 03 | CAT | GATATT AACC GGTTCCGCGG | ATCCCATGCA TG | 27 |
| 88 | | B CATGGAACTA | GATAAT AACC GGTCCCGCGG | GTACAATGCA TG | |
| 68 | PPI | ATA | GTTATA GCAG GGTATGGAAT | GIGCGCGCG ATG | 28 |
| 06 | | AAG | | AGCAGCGCAC ATG | |
| 91 | GSAT | ATC | | GCCTGCTGCC GTG | 28 |
| 92 | | ATC | ATTAAA TTAC GGGGGGTACA | ACCIGCIGCC GIG | 1 1 1 1 1 1 |
| 93 | ORF 05 | CCI | | GCGGCTGCGC ATG | 28 |
| 94 | | ACT | | TCGTCCGCGC ATC | |
| 95 | deaminase | 9 | CATAAT ATGC CGGGCGGTGG | CACCATGGCC GTTO | 29 |
| 96 | | ၅ | CATAAT ATGC CGGGCGGGG | CAGGCIGCCC .GTG | |
| 76 | RNA halic | TGT | | CAGGGCCGCG CGTG | 29 |
| 86 | | 990 | CATAAA ACAA CAGGCCGCGG | CAGGGCG.CG CGTG | |
| თ | ORF 06 | Α. | TATAAA CGGG GGCCCGGGCG | GCGCGTATCA CATG | 29 |
| 100 | | | TATAAA CAGA GG.CCGGACG | | 1 1 1 1 1 1 |
| 101 | tRNA-tyr | | TTTAAA ACTA GGATGCCGAT | CACGGATCGT CCCA | 29 |
| 102 | | TCI | TTTAAA ACTA GGATGCCGGG | | |
| 103 | TBP | ပ္ပ | GTIAAA ATAG CG.CACGGGC | | UE ======= |
| 104 | | | GTTAAA ATAG AGTGCGGCCG | _ | ŀ |
| 105 | TIM | 909 | AATAAA TACG CGCAGGGGC | CCCGTGGCGC GATCGCCCGT | 989 |
| 106 | | | AATAAA TACG CGC.GGGGCC | GCGGTGC GATCGCCCGT | 1 |
| 107 | Hypoth 01 | ATT | CATAAA TGCC TAGTTACGCA | Ø | TCGACTAATG 49 |
| 108 | | ACT | CATAAA TGCC TAGCTACCCA | GAAATATCAA ACAAAQTACT | • |
| 109 | 04F C1 | ACG | ATTAIT ACCT IGCCTIGGGT | TGTA //G CGGGGTGCGG | CAGGGGATG 52 |
| 110 | | ACG | ATTAIT ACCI IGCCGIGIG. | | • |
| 111 | Methyiase | | TITAAG TCGG CGCCGGGCA | GCCG.//G ATGTGGGGCA | GGCAACATE 104 |
| 112 | | | TITAAG ACGG CGCGGGTGCC | _ | |
| 113 | 168 RNA | TCG | | CCGATCCGAT CGTACGTGAC | GC. ' ' AAT 220 |
| 114 | | | TITAIA IGCC CAIGGACAAG | GCGATCCGAT CGTACGTGAC | GC.//AAT |
| Archaeal | l promoter | | | | |
| consensus | 7) | | yttama FIC 9 | | |

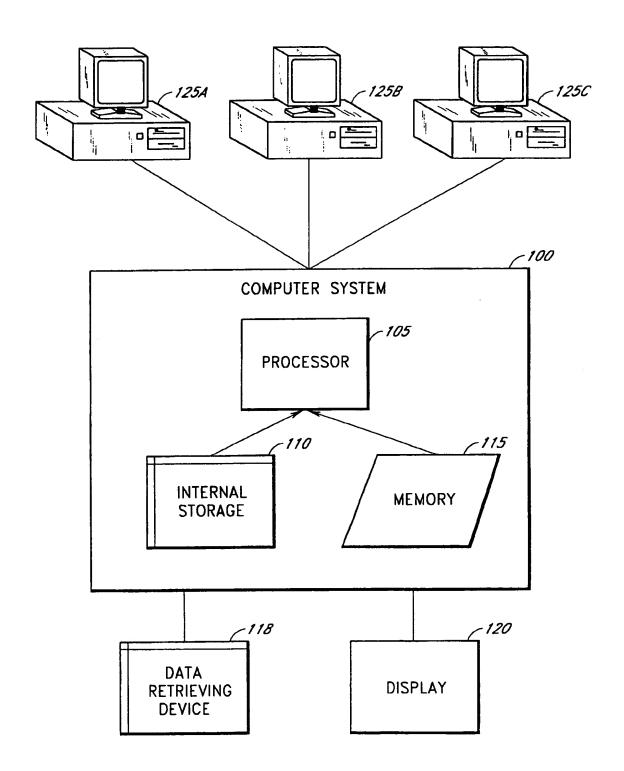


FIG.3

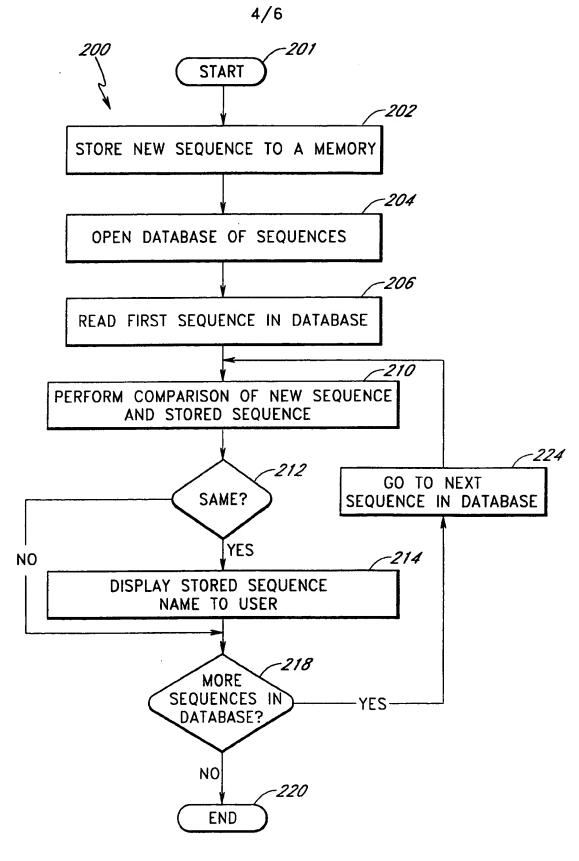


FIG.4

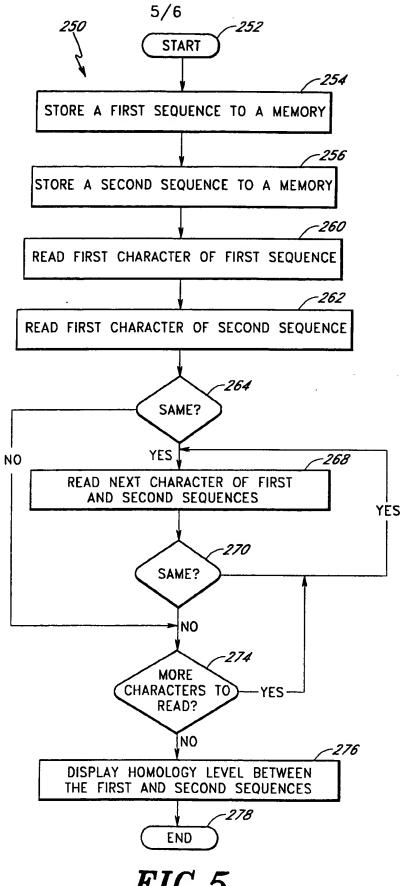


FIG.5

PCT/US99/22752

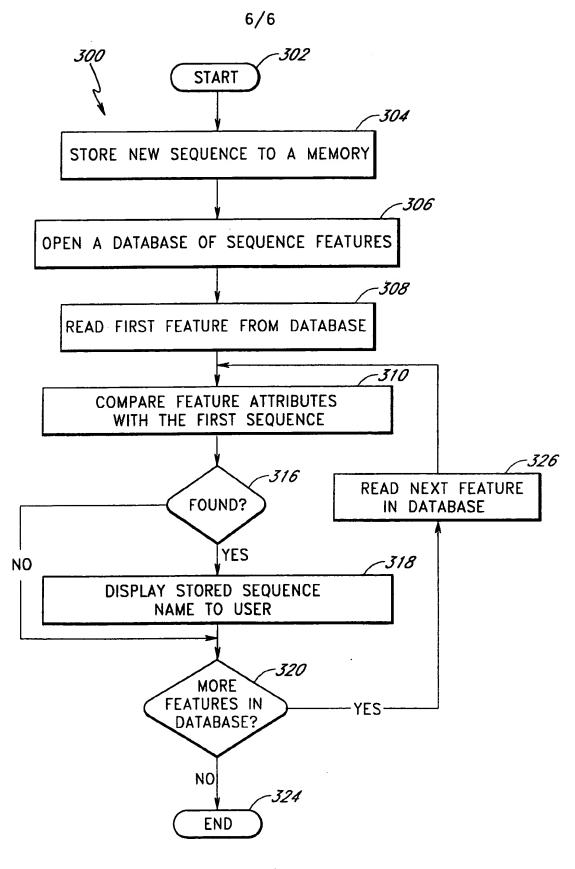


FIG.6

-1-

SEQUENCE LISTING

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| gtaacaaacg | actccgaggt | ctcgcttgac | ttttgggagt | atgtgaaaaa | agagtacgtc | 39840 |
| gggggcggcg | tgatccaggc | aggcgacata | tcctccggat | accactgcat | gaagcccgcc | 39900 |
| tatctagagg | accagctgaa | gaggagcctt | gcaaacatgg | gcctcgactg | tatcgacctt | 39960 |
| | | cgaggggcag | | | | 40020 |
| gactgtatag | gagaggcctt | tgccatgtac | gagaaggcaa | gggaggatgg | ccgcatcaga | 40080 |
| | | ggagtgcttt | | | | 40140 |
| cagctcgaag | acgttgtaaa | gaaggccaaa | gacgcaggcg | gggacaacca | cggattcaag | 40200 |
| ttcatacagc | tgcccttcaa | ccagtacttt | gaccaggctt | acatgctaaa | gaaccagacg | 40260 |
| | | catactggat | | | | 40320 |
| acgagtgtcc | cgttcatgca | aggcaagctg | ctcgagcctg | gcctgctgcc | ggagtttggc | 40380 |
| | | atccctgcag | | | | 40440 |
| cccctgccgg | ggcacaactc | agctgcgcat | acagacgaga | acctcaagat | catgggcgtg | 40500 |
| cccccatcc | cgcctgacaa | gttcggggag | cttgtggcca | gcctcacctc | gtggtcgccc | 40560 |
| ggtcagaaat | agccggtcag | ctgcctctcg | ggcattatct | ggtcgagcac | cttttttgag | 40620 |
| agccgtgaat | cggcggaatc | ctgcacgttg | cgccgggccc | ttgccacgtt | ggcaggatac | 40680 |
| aggtctatcc | cggtaaagcc | cctcttgagg | catgcagaga | ctattcccgt | ggtccccctg | 40740 |
| cctgcaaacg | ggtccagcac | gtaatcgccc | tcttttgtgg | caaactttac | tatcctggat | 40800 |
| acaaggtctt | ctgggaatac | cgcaaagtgc | tcgtttccat | ggtgcgcctt | tgtggatatc | 40860 |
| tcccagacgt | tccccgggtt | cttgccccgc | gggttgcatg | cggcaaatat | cggatagtgc | 40920 |
| tcgtggcccc | ctatcctctt | gcgcgtcgca | tgcctccgga | acttgcgata | gcacgtgggg | 40980 |
| cagtactttt | cggggtcata | gccgtgggcc | catgatattt | ccccggtggt | tggcagctcg | 41040 |
| | | | | | | |

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tcaaacggcg taccaggcgt tgagccgtgt atcacggctg caatcctccc tattgcctcg 41100 ggatccctct tcccgggggc gaactgcagc cggtcatttg cgggtttgct gtttatcccg 41160 ctcagggcct cgttgccctg gacgcgtatc gggtttatgt cataggcggg ggtatccgac 41220 tttgagagga ccagaacaaa ctcgtacgcc tgcgtcaggt tttgccgcga gctttgcgag 41280 atggcgtttc gcttgtacca gattatatcc tcctggaaat ggtacccaag atccaccagc 41340 cttagcgcga gccggtgcgg gaccatcagc ttgtggcgcc gcctcctggt atcacctatc 41400 actatgaaga ggctcccgtc gtctgttagc aggtccatgc agctcttgaa tactcctgcc 41460 agetectega tgaactegte tggegtettt teetggeeca geteggaggg eteegaeeeg 41520 tactttctgt gcccgtaata gggaggggat gttaccgcca gtctgtacct gccgcgctcg 41580 41640 getgtattet ttgccagecg eggeageace teeegggegt egeeetgeag tatetggaac ttttcactca agataggccc ccgtgccatc catctgcccc tgcgcgatcc gacaagtcgt 41700 atteatettg tacegeggea ecegegeegt ettaaaatet ttgtagetta taceggegeg 41760 ccgcagatgc ggtacaatcc ctccggtgct cccgcgatcc ggcgcggtgc catcagccgc 41820 cccgtttccc cttccggggg ccccgccacc atacacgtgg tataaacaga ggccggacgg 41880 41940 cgcggaccac atgtggataa aggacgagtt tcttggcaaa ggcaacaaga tgaggctgct ctacatcata ctgcccatct acgggtacct cttcctggag tactggccgt tcctgccctg 42000 gatggctaca ttctggtggt cggtggcgct cagcccccct attctcctga tgccttatgc 42060 cggggaggcc ataggtcagc tgatcggcgg gcatgtattg tttggagttg tcacaaagta 42120 tgtctatgcg gcagtatggc tgggcatggc acacgggata atcctcctga cagggcgcct 42180 cagggccagg gctggtaccc tgcgcgaatc ccccgcatag ccccggcagg gcccgttgtt 42240 ccggatggcc aaggccggcg catacatccc atgatgcata gaccgggggg acatgatcgc 42300 agcagatogt tocatgoogo cocegtacgo totggggego acctagtoag ggcggggeco 42360 cccgcggtcc aattaaatac ggcaaggaac ggggggtctc gttgaaactg cagggcagga 42420 42432 ctgccgtgat cc <210> 3 <211> 10419 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(10419) <400> 3 atc ccc gcg ccg cca gga gag ggc agc ctt ggc ggg gtg gca ata tcc 48 Met Pro Ala Pro Pro Gly Glu Gly Ser Leu Gly Gly Val Ala Ile Ser 15 qac gac ggg agg tac atg tac gca atc ggc agg gat ctg ctc aca gta 96 Asp Asp Gly Arg Tyr Met Tyr Ala Ile Gly Arg Asp Leu Leu Thr Val 20 tac egg tat aca atg aac eeg eec cat gac ata gee teg gee geg etc 144 Tyr Arg Tyr Thr Met Asn Pro Pro His Asp Ile Ala Ser Ala Ala Leu 35 ggt gcg cag tca ttt tct ctg cct ggc ggc atc agc ccc gcc ccc ggc 192 Gly Ala Gln Ser Phe Ser Leu Pro Gly Gly Ile Ser Pro Ala Pro Gly 55 240 geg eeg ace gge ett gae ate teg gat gae gge ege eac etg tae gte Ala Pro Thr Gly Leu Asp Ile Ser Asp Asp Gly Arg His Leu Tyr Val ccg gac gaa aac ggc gtc gtg tac agg ttt gat ctg gaa agc ccg tac 288 Pro Asp Glu Asn Gly Val Val Tyr Arg Phe Asp Leu Glu Ser Pro Tyr

90

85

| agg
Arg | cta
Leu | gac
Asp | ggc
Gly
100 | ggc
Gly | acg
Thr | ttt
Phe | ggc
Gly | tct
Ser
105 | tct
Ser | gtt
Val | tat
Tyr | gtg
Val | gga
Gly
110 | tcc
Ser | gac
Asp | 336 |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gtt
Val | gcc
Ala | gcg
Ala
115 | ccc
Pro | cgc
Arg | ggc
Gly | gta
Val | tac
Tyr
120 | gtg
Val | gcg
Ala | ccg
Pro | ggc
Gly | ggc
Gly
125 | agc
Ser | ctc
Leu | atg
Met | 384 |
| ctg
Leu | gtc
Val
130 | tcg
Ser | gat
Asp | agt
Ser | gca
Ala | gac
Asp
135 | ggc
Gly | acc
Thr | atc
Ile | cac
His | agg
Arg
140 | tac
Tyr | gag
Glu | ctg
Leu | gca
Ala | 432 |
| agc
Ser
145 | ccg
Pro | tac
Tyr | gag
Glu | ccg
Pro | gcg
Ala
150 | ggc
Gly | gcg
Ala | gca
Ala | aac
Asn | agg
Arg
155 | gga
Gly | tca
Ser | ttc
Phe | gac
Asp | gtg
Val
160 | 480 |
| tcg
Ser | gat
Asp | atg
Met | gac
Asp | ggc
Gly
165 | tcg
Ser | cct
Pro | gtc
Val | ggg
Gly | gcg
Ala
170 | ggg
Gly | ttt
Phe | gcg
Ala | ggc | ggc
Gly
175 | ctg
Leu | 528 |
| cac
His | atg
Met | tat
Tyr | gtc
Val
180 | gcg
Ala | gga
Gly | aac
Asn | gac
Asp | acc
Thr
185 | gga
Gly | agg
Arg | gtc
Val | tac
Tyr | cag
Gln
190 | tat
Tyr | ccg
Pro | 576 |
| gcg
Ala | ggc
Gly | acg
Thr
195 | cac
His | cag
Gln | ata
Ile | cag
Gln | gag
Glu
200 | gca
Ala | gcc
Ala | gca
Ala | Gly
ggg | ccg
Pro
205 | cgg
Arg | ctg
Leu | ctc
Leu | 624 |
| tcg
Ser | gcc
Ala
210 | gtc
Val | ctg
Leu | gac
Asp | aaa
Lys | gac
Asp
215 | gga
Gly | acc
Thr | ctg
Leu | agg
Arg | gcg
Ala
220 | gcc
Ala | ttt
Phe | gac
Asp | ggc
Gly | 672 |
| acg
Thr
225 | gta
Val | gac
Asp | gcg
Ala | gga
Gly | tcc
Ser
230 | gtg
Val | cag
Gln | ccc
Pro | G1 A
aaa | atg
Met
235 | atc
Ile | acc
Thr | atc
Ile | agg
Arg | gac
Asp
240 | 720 |
| | | | | | | | ata
Ile | | | | | | | | | 768 |
| gcg
Ala | gac
Asp | tct
Ser | gat
Asp
260 | gtc
Val | atg
Met | aca
Thr | ttt
Phe | gtg
Val
265 | gtc
Val | ccc
Pro | gag
Glu | aaa
Lys | gac
Asp
270 | agg
Arg | gca
Ala | 816 |
| | | | | | | | cag
Gln
280 | | | | | | | | | 864 |
| ctg
Leu | gcg
Ala
290 | G] y
ggg | act
Thr | ggc
Gly | ggc
Gly | ggg
Gly
295 | ccg
Pro | ttt
Phe | gtg
Val | ccc
Pro | gac
Asp
300 | ttt
Phe | tcc
Ser | Gly
999 | ggc
Gly | 912 |
| | | | | | | | cgg
Arg | | | | | | | | | 960 |
| gag | atg | gca | cgg | acg | gag | aga | tcc | gac | agg | tac | gcg | ctt | act | gta | act | 1008 |

| Glu | Met | Ala | Arg | Thr
325 | Glu | Arg | Ser | Asp | Arg
330 | туr | Ala | Leu | Thr | Val
335 | Thr | |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| gca
Ala | ggc
Gly | Gly
333 | agt
Ser
340 | cag
Gln | atg
Met | cat
His | gtg
Val | ggc
Gly
345 | ggc
Gly | gcc
Ala | ggc
Gly | gga
Gly | aac
Asn
350 | atc
Ile | acc
Thr | 1056 |
| tgg
Trp | tac
Tyr | gat
Asp
355 | ctt
Leu | ggc
Gly | acg
Thr | ccc
Pro | cat
His
360 | gac
Asp | ata
Ile | acg
Thr | acc
Thr | ggc
Gly
365 | gtc
Val | cgc
Arg | gcg
Ala | 1104 |
| gga
Gly | tcc
Ser
370 | gac
Asp | atc
Ile | ctg
Leu | ccg
Pro | gcg
Ala
375 | tat
Tyr | cca
Pro | tcc
Ser | gcg
Ala | ggc
Gly
380 | aga
Arg | aac
Asn | gtg
Val | gtg
Val | 1152 |
| ccg
Pro
385 | tca
Ser | ata
Ile | acg
Thr | ggc
Gly | att
Ile
390 | gcc
Ala | ttc
Phe | tcg
Ser | gat
Asp | gac
Asp
395 | ggc
Gly | atg
Met | cgg
Arg | ttg
Leu | ttt
Phe
400 | 1200 |
| gca
Ala | gca
Ala | aac
Asn | cgg
Arg | ggc
Gly
405 | gac
Asp | cgc
Arg | att
Ile | cca
Pro | atg
Met
410 | tac
Tyr | cag
Gln | ctg
Leu | gac
Asp | agc
Ser
415 | ccg
Pro | 1248 |
| tac
Tyr | gac
Asp | ata
Ile | ggg
Gly
420 | agc
Ser | gcc
Ala | agc
Ser | ctc
Leu | gag
Glu
425 | gga
Gly | acc
Thr | ctg
Leu | ttt
Phe | acg
Thr
430 | Gly
aaa | ttc
Phe | 1296 |
| | | | | | ttc
Phe | | | | | | | | | | | 1344 |
| ctg
Leu | ctc
Leu
450 | acc
Thr | gag
Glu | aat
Asn | gcc
Ala | ata
Ile
455 | cgg
Arg | cag
Gln | tac
Tyr | gac
A sp | ctg
Leu
460 | gag
Glu | ggc
Gly | ccc
Pro | tat
Tyr | 1392 |
| gac
Asp
465 | ata
Ile | cgc
Arg | G] À
aaa | gcg
Ala | ggc
Gly
470 | aat
Asn | gcg
Ala | ggc
Gly | cag
Gln | tac
Tyr
475 | gac
Asp | ctg
Leu | gac
Asp | atc
Ile | ccg
Pro
480 | 1440 |
| ctg
Leu | cac
His | cca
Pro | gga
Gly | ctg
Leu
485 | ctg
Leu | ttc
Phe | ctg
Leu | ctg
Leu | acc
Thr
490 | tcg
Ser | Gly
ggg | gtg
Val | cac
Kis | ttt
Phe
495 | tcg
Ser | 1488 |
| | | | | | atg
Met | | | | | | | | | | | 1536 |
| gat
Asp | gcc
Ala | aac
Asn
515 | gcg
Ala | aac
Asn | agg
Arg | gat
Asp | gtc
Val
520 | aac
Asn | gtc
Val | aac
Asn | ctg
Leu | tgg
Trp
525 | cac
His | agg
Arg | ttt
Phe | 1584 |
| | | | | | ttt
Phe | | | | | | | | | | | 1632 |
| | | | | | ggg
Gly
550 | | | | | | | | | | | 1680 |

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| | | | | | aga
Arg | | | | | | | | | | | 1728 |
|-----|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-----|------------|------------|------------|------------|-----|------|
| | | | | | atc
Ile | | | | | | | | | | | 1776 |
| | | | | | ccg
Pro | | | | | | | | | | | 1824 |
| | | | | | gac
Asp | | | | | | | | | | | 1872 |
| | | | | | acg
Thr
630 | | | | | | | | | | | 1920 |
| His | Leu | Asn | Pro | Pro
645 | ttt
Phe | Asp | Val | Gly | Thr
650 | Ala | Val | Phe | His | Asp
655 | His | 1968 |
| Gly | Arg | Phe | Arg
660 | Pro | Gly
999 | Gly | Pro | Ala
665 | Ser | Glu | Ile | Glu | Ala
670 | Ser | Gly | 2016 |
| Ile | Ser | Leu
675 | Ser | Ala | gac
Asp | Gly | Ser
680 | Arg | Met | Phe | Leu | Ser
685 | Asp | Arg | Glγ | 2064 |
| Arg | Gly
690 | Ala | Ile | Ser | cag
Gln | Tyr
695 | Thr | Leu | Val | Ala | Pro
700 | Phe | Asp | Val | Glu | 2112 |
| | | | | | tcc
Ser
710 | | | | | | | | | | | 2160 |
| Asp | Ala | Leu | Pro | Gly
725 | G] A
G3A | Leu | Ala | Phe | Ser
730 | Pro | Gly | Gly | Thr | Arg
735 | Leu | 2208 |
| | | | | | atg
Met | | | | | | | | | | | 2256 |
| Thr | Pro | Phe
755 | Asp | Leu | ggc | Gly | Ala
760 | Glu | His | Ala | Ala | Ser
765 | Phe | Gly | Val | 2304 |
| | | | _ | _ | gat
Asp | | | | | | | | | | | 2352 |
| act | aaa | atg | cta | ata | gcc | gat | acg | aca | ggc | ttt | gtg | cac | aaa | tac | gac | 2400 |

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| Thr
785 | _ | Met | Leu | Ile | Ala
790 | _ | Thr | Thr | Gly | Phe 795 | | . His | Gly | Tyr | Asp
800 | |
|------------|---|-----|-----|-----|------------|---|-----|-----|-----|---------|---|--------------------|-----|-----|------------|------|
| | | _ | _ | | _ | | _ | | | Ala | | agc
Ser | | | Phe | 2448 |
| _ | _ | | | _ | | | _ | | Ala | - | | Gly | | Ser | atg
Met | 2496 |
| | | | | | | _ | - | | | | | cac
His
845 | _ | | ggc
Gly | 2544 |
| | | _ | | _ | | _ | _ | _ | | _ | | ctg
Leu | _ | | _ | 2592 |
| | | | | | | | | | | | | ttt
Phe | | _ | | 2640 |
| | | | | | | | | | | | | ata
Ile | | - | - | 2688 |
| | | | | | | | | | | | | gtc
Val | | | | 2736 |
| _ | | | | | - | | | _ | _ | _ | _ | gcg
Ala
925 | | _ | | 2784 |
| | | | | | | | | | | | | gga
Gly | _ | | | 2832 |
| | | | | | | | | | | | | ata
Ile | | | | 2880 |
| | | | | | | | | | | | | gat
Asp | | | | 2928 |
| | | | | | | | | | | | | gtg
Val | | | | 2976 |
| | | | Pro | | | | | Tyr | | | | ctg
Leu
1005 | Asn | | | 3024 |
| Phe | _ | Ile | _ | | | | Pro | | | | _ | atc
Ile | | | _ | 3072 |

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| | | Val | | | | | Phe | | | | | Arg | | | cta
Leu | | 3120 |
|---|-------------|-----|-----|-----|-----|-----|-----|-----|-------------|-----|-----|-----|-----|-----|--------------------|-----|------|
| | | | | | | Gly | | | | | Leu | | | | ccg
Pro
1055 | Tyr | 3168 |
| | | | | | Asp | | | | | Ser | | | | | gtc
Val | | 3216 |
| | | | | Ala | | | | | Gln | | | | | Ile | gcc
Ala | | 3264 |
| | | | Asp | | | | | Leu | | | | | Ser | | tct
Ser | | 3312 |
| | | Arg | | _ | _ | | Ser | _ | | - | - | Ser | | | aaa
Lys | | 3360 |
| | | | | | _ | Ile | | | | | Ser | | | | ttc
Phe
1135 | Ser | 3408 |
| | | | | | Arg | | | | | Asp | | | | | acg
Thr | | 3456 |
| | - | | | Gly | | | _ | | Tyr | | | | | Ala | gag
Glu | | 3504 |
| | | | Pro | | | | | Val | | | | | Ala | | ctc
Leu | | 3552 |
| | | qaA | | | | | Leu | | | | | Pro | | | tcc
Ser | | 3600 |
| | | | | | | Thr | | | | | Cys | | | | cgg
Arg
1215 | Gly | 3648 |
| | | - | | | Ser | _ | _ | _ | | Ile | | _ | | | agt
Ser | _ | 3696 |
| | | | | Glu | | _ | _ | | Ala | - | _ | Ile | _ | Ala | gca
Ala | _ | 3744 |
| , | 9 99 | cca | gga | att | ggc | gag | ctg | cac | 9 99 | ttt | gca | ggc | ccg | ccg | atg | ccg | 3792 |

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| Gly Pro Gly Ile Gly Glu Leu His Gly Phe Ala Gly Pro Pro Met Pro
1250 1255 1260 | |
|---|------|
| gcg cct gtc atg gag cag gtc aca ctg gat tcg cgg gag ggc aca ctc
Ala Pro Val Met Glu Gln Val Thr Leu Asp Ser Arg Glu Gly Thr Leu
1265 1270 1275 1280 | 3840 |
| agg gtc agg ctg gac agg aca gtg gac gtc gac acg gtg cgc ccc tat
Arg Val Arg Leu Asp Arg Thr Val Asp Val Asp Thr Val Arg Pro Tyr
1285 1290 1295 | 3888 |
| aag atg tgg gtg gag gat tca gac ggc agc cag aca acc ctg gca aat
Lys Met Trp Val Glu Asp Ser Asp Gly Ser Gln Thr Thr Leu Ala Asn
1300 1305 1310 | 3936 |
| tca aca ctg ttg aat gcc gaa aac tcg aac att ctg ctc ttc agg ctg
Ser Thr Leu Leu Asn Ala Glu Asn Ser Asn Ile Leu Leu Phe Arg Leu
1315 1320 1325 | 3984 |
| gat gat gcg gcc gca ggc aaa ata tcc ggg tat aca tcc ccc gtg ttt
Asp Asp Ala Ala Ala Gly Lys Ile Ser Gly Tyr Thr Ser Pro Val Phe
1330 1335 1340 | 4032 |
| cgc acg tgg tcg tcg ccg ttc ctg ggc aca gac gga gcc acc agg ccc
Arg Thr Trp Ser Ser Pro Phe Leu Gly Thr Asp Gly Ala Thr Arg Pro
1345 1350 1355 1360 | 4080 |
| cat acg ctg ggc ttt gga gac gtg cgc ctt gcg gat ata tac gat gca
His Thr Leu Gly Phe Gly Asp Val Arg Leu Ala Asp Ile Tyr Asp Ala
1365 1370 1375 | 4128 |
| tcc ggg gat gtc ccg tcg ccg tcg ggc att gag ttt tca gat gac ggc
Ser Gly Asp Val Pro Ser Pro Ser Gly Ile Glu Phe Ser Asp Asp Gly
1380 1385 1390 | 4176 |
| atg agg atg ttc gtt acg ggg atc ggc acg cca ggc atc aac ata ttc
Met Arg Met Phe Val Thr Gly Ile Gly Thr Pro Gly Ile Asn Ile Phe
1395 1400 1405 | 4224 |
| aca ctg tcc gcc ccc ttt gac ata aca ttg ccg aag cat tcc ggc tca
Thr Leu Ser Ala Pro Phe Asp Ile Thr Leu Pro Lys His Ser Gly Ser
1410 1415 1420 | 4272 |
| acc aac ata ggc ggc ctg tcc gtg tct gat ctg gca ttt gca aac aat
Thr Asn Ile Gly Gly Leu Ser Val Ser Asp Leu Ala Phe Ala Asn Asn
1425 1430 1435 1440 | 4320 |
| ggg aac agc ctc acg gtg ctc gat gtg gac ggg gtg ttg cgc gtc tac
Gly Asn Ser Leu Thr Val Leu Asp Val Asp Gly Val Leu Arg Val Tyr
1445 1450 1455 | 4368 |
| gcc ctt ggg gac gat tac aat gtg gtc acc gga acc acc cag aag ttt
Ala Leu Gly Asp Asp Tyr Asn Val Val Thr Gly Thr Thr Gln Lys Phe
1460 1465 1470 | 4416 |
| agg att acg ctc gat acc aca cag ggc ata ccc aat tcc att tac aca
Arg Ile Thr Leu Asp Thr Thr Gln Gly Ile Pro Asn Ser Ile Tyr Thr
1475 1480 1485 | 4464 |

| | _ | Asp | | _ | | _ | Phe | | | | | Asp | | | gac
Asp | 4512 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------------------|-----|-----|-----|-----|--------------------|------|
| _ | Tyr | | | | _ | Pro | | _ | | tcg
Ser
151 | Ser | | | | ata
Ile
1520 | 4560 |
| | _ | | _ | _ | Pro | | _ | _ | _ | cca
Pro
0 | | | _ | _ | Phe | 4608 |
| _ | | _ | | Arg | | _ | | _ | Ser | acc
Thr | | | | Ile | _ | 4656 |
| _ | | - | Leu | | _ | _ | | Ala | _ | acc
Thr | - | _ | Val | | _ | 4704 |
| _ | _ | Ile | | | _ | | Gly | | | gga
Gly | | Arg | | - | - | 4752 |
| | Gly | | | | | Val | | | | gac
Asp
1599 | Gly | | | | | 4800 |
| | | | | | Pro | | | | | acg
Thr | | | | | Thr | 4848 |
| | | _ | | Val | - | _ | | | Pro | ggc
Gly | | | | Ala | _ | 4896 |
| | | | Arg | | | | | Phe | | gca
Ala | | | Asn | | | 4944 |
| - | _ | Ser | | | | | Ser | | _ | ggc
Gly | _ | Gly | _ | | _ | 4992 |
| | Gly | | | _ | | Gly | | | | ttc
Phe
1675 | Ser | | | | | 5040 |
| | | | | | Pro | | | | | ttg
Leu
) | | | | | Gly | 5088 |
| | | - | _ | Asp | _ | | | | Glu | gat
Asp | - | | | Leu | _ | 5136 |
| ttg | ctg | gcc | gcg | gat | gga | aca | ctg | gat | ttc | tac | agc | ctt | gcc | ggt | gat | 5184 |

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| Leu | ı Let | 1 Ala
171 | | Asp | Gly | Thr | Leu
172 | | Phe | г Туг | : Ser | Leu
172 | | a Gly | / Asp | |
|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|------|
| | | qeA | | | | | Ser | | | | | Val | | | gag
Glu | 5232 |
| | Ala | | | | | Pro | | | | | Gln | | | | ggc
Gly
1760 | 5280 |
| | | | | | Ala | | | | | Ile | | | | | gtg
Val
5 | 5328 |
| | | | | Phe | | | | | Leu | | | | | Thr | ccc
Pro | 5376 |
| aca
Thr | Gly | att
Ile
179 | Asp | ttt
Phe | gcg
Ala | cca
Pro | gac
Asp
180 | Gly | cgc
Arg | tgg
Trp | atg
Met | ttc
Phe
180 | Leu | tcc
Ser | acc
Thr | 5424 |
| gag
Glu | aac
Asn
181 | Gly | ata
Ile | gac
Asp | cag
Gln | tac
Tyr
1815 | Leu | ctg
Leu | tcg
Ser | atc
Ile | ccc
Pro
1820 | Phe | gac
Asp | gtg
Val | cgc
Arg | 5472 |
| agc
Ser
1825 | Leu | acg
Thr | tat
Tyr | acg
Thr | gga
Gly
1830 | Thr | att
Ile | cca
Pro | gta
Val | gac
Asp
1839 | Gly | gtg
Val | gag
Glu | gga
Gly | atg
Met
1840 | 5520 |
| cag
Gln | ttt
Phe | gcg
Ala | gac
Asp | aac
Asn
1845 | Gly | agg
Arg | gca
Ala | ctg
Leu | ttt
Phe
1850 | Leu | gcg
Ala | gac
Asp | agt
Ser | gaa
Glu
1859 | Gly | 5568 |
| ttg
Leu | att
Ile | tac
Tyr | aat
Asn
1860 | Tyr | gac
Asp | ctg
Leu | gag
Glu | gac
Asp
1865 | Pro | tat
Tyr | gct
Ala | ctg
Leu | gat
Asp
1870 | ggc
Gly | aac
Asn | 5616 |
| aca
Thr | att
Ile | tcc
Ser
1875 | Val | gaa
Glu | ttc
Phe | tcg
Ser | ttt
Phe
1880 | Asp | ggt
Gly | agc
Ser | gtg
Val | atg
Met
1885 | Tyr | gtg
Val | ctg
Leu | 5664 |
| gag
Glu | tac
Tyr
1890 | qaA | aca
Thr | aaa
Lys | Arg | gtg
Val
1895 | gtc
Val | tcg
Ser | tac
Tyr | gag
Glu | ttg
Leu
1900 | Glu | ttt
Phe | ccc
Pro | ttt
Phe | 5712 |
| gac
Asp
1905 | Val | tcg
Ser | agc
Ser | Arg ' | aca
Thr
1910 | cgt
Arg | gca
Ala | gac
Asp | acg
Thr | ctg
Leu
1915 | qaA | ata
Ile | cca
Pro | caa
Gln | att
Ile
1920 | 5760 |
| gac
Asp | tca
Ser | cca
Pro | Arg : | cac (
His ' | gtt (
Val . | gca (
Ala | gtc
Val | Ser | atg
Met
1930 | Pro | ggc
Gly | aac
Asn | His | ctg
Leu
1935 | Tyr | 5808 |
| ata
Ile | aca
Thr | Asn . | tcg g
Ser ' | gtg 1
Val 1 | ttt (
Phe (| ggg 9
Gly 0 | Glu . | gat
Asp
1945 | gac
Asp | acc
Thr | ata (| His | tcc
Ser
1950 | Tyr | gga
Gly | 5856 |

| | | | Asn | | | | | Ala | tca
Ser | | | | Glu | | ggc
Gly | 5904 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|--------------------|-----|-----|-----|-----|-----|------------|------|
| | | Glu | | | | | Gly | | gac
Asp | | | Asn | | | | 5952 |
| | Met | | | | | Gly | | | ttc
Phe | | Tyr | | | | | 6000 |
| _ | | _ | | | Thr | | | | ata
Ile
2010 | Ser | | | | | Leu | 6048 |
| | | | | Ile | | | | | gtt
Val | | | | | Leu | | 6096 |
| | | | Asp | | | | | Phe | ata
Ile | | | | Ala | | | 6144 |
| | | Arg | | | | | Asp | | ttc
Phe | | | Glu | | | | 6192 |
| | Gln | | | | | Leu | | | cca
Pro | | Ala | | | | | 6240 |
| | | | | | Phe | | | | ggc
Gly
2090 | Leu | | | | | Ser | 6288 |
| | | | | qaA | | | | | ttt
Phe | | | | | Pro | | 6336 |
| | - | _ | Leu | _ | | | | Leu | gag
Glu | | | | Val | | | 6384 |
| _ | _ | Gly | | | | _ | Asp | | ggg
Gly | - | - | Leu | | | | 6432 |
| | Phe | _ | _ | | | Ser | _ | | ggc
Gly | | Leu | | _ | | _ | 6480 |
| _ | - | | _ | | Gly | | | | gac
Asp
2170 | Leu | | _ | | | Phe | 6528 |
| gcg | cag | tcc | ctg | gga | ata | ttc | gat | ttt | cct | ccc | ttc | aac | ggc | atg | cgg | 6576 |

| Ala | Gln | Ser | Leu
218 | _ | Ile | Phe | Asp | Phe
218 | | Pro | Phe | Asn | Gly
219 | Met
O | Arg | |
|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|--------------------|-----|------|
| _ | | | Ser | _ | _ | | | His | | _ | | - | Gly | agc
Ser | | 6624 |
| _ | | Arg | _ | | | - | Glu | _ | | - | | Ser | | gac
Asp | _ | 6672 |
| - | Ser | | _ | _ | _ | Thr | | | | | Glu | | | aaa
Lys | | 6720 |
| | | | | | Thr | | | | | Asp | | | | tcc
Ser
225 | Pro | 6768 |
| _ | | _ | | Leu | | - | | | Gly | | - | _ | _ | atg
Met
O | | 6816 |
| | | | Asp | _ | | _ | | Asp | - | _ | _ | | Ala | ggt
Gly | | 6864 |
| _ | _ | Leu | _ | | | | Val | | | | | Ile | | ttc
Phe | | 6912 |
| | Asp | | _ | _ | _ | Phe | _ | | | _ | Asp | | _ | cac
His | | 6960 |
| | | | | | Asn | | | | | Ile | | | | ata
Ile
2335 | Leu | 7008 |
| | | | | Ser | | | | | Asn | | | | | gly
ggg | | 7056 |
| | | | Glu | | | | | Ala | | | | | Gly | cgt
Arg | | 7104 |
| | - | Thr | | | _ | | Leu | _ | | | | Leu | | ggc | | 7152 |
| | Ser | _ | _ | _ | _ | Ala | _ | | | _ | Tyr | | | gag
Glu | | 7200 |
| | | | | | Asp | | | | | Asp | | | | cgc
Arg
2415 | Met | 7248 |

-35ttc gtg gcg ggc gta aac aac cat tta aga cag tac aac ctg ctg tcg 7296 Phe Val Ala Gly Val Asn Asn His Leu Arg Gln Tyr Asn Leu Leu Ser ccg tat gac act gaa aat gca gaa cat ttc atc tcg acg gat ctg ctg 7344 Pro Tyr Asp Thr Glu Asn Ala Glu His Phe Ile Ser Thr Asp Leu Leu 2435 2440 act gcg gac agg ggc ccc acg ggt ctt gta ttt tca gat gag aac gac 7392 Thr Ala Asp Arg Gly Pro Thr Gly Leu Val Phe Ser Asp Glu Asn Asp 2450 2455 2460 ttt ttc agc aca ggc gcc agg gcc caa ttt gtg cgc cag ttt acg aca 7440 Phe Phe Ser Thr Gly Ala Arg Ala Gln Phe Val Arg Gln Phe Thr Thr 2465 2470 2475 aac cgc ccg tac gac gca tcc aca ata aca ctg agt gac aac gga ctq 7488 Asn Arg Pro Tyr Asp Ala Ser Thr Ile Thr Leu Ser Asp Asn Gly Leu 2485 2490 2495 tac aag gtg agc gtg gac ggc ctg ccg tcc ggc ata cgg ttt acc ccc 7536 Tyr Lys Val Ser Val Asp Gly Leu Pro Ser Gly Ile Arg Phe Thr Pro 2500 gac ggc atg aag atg ttc ata teg ggc cag gag acg gcc atg ata tac 7584 Asp Gly Met Lys Met Phe Ile Ser Gly Gln Glu Thr Ala Met Ile Tyr 2520 cag tat tcc ctg ccg tcc ccg tat gac aca tcc ggg gcg gtc agg gac 7632 Gln Tyr Ser Leu Pro Ser Pro Tyr Asp Thr Ser Gly Ala Val Arg Asp 2535 agg gtt gag ata gtc gca ggg ctc ttt aga aat gca ggt ttg tcc gtc 7680 Arg Val Glu Ile Val Ala Gly Leu Phe Arg Asn Ala Gly Leu Ser Val 2545 2550 2555 ggg ttg aac gag ccc agt cct tcc ggc ttt gac ttt tcg gag gac gga 7728 Gly Leu Asn Glu Pro Ser Pro Ser Gly Phe Asp Phe Ser Glu Asp Gly 2565 2570 atg gag ctg tac gtg acg ggg tcg ggc ctt gtt cac agg tat ttc ctg 7776 Met Glu Leu Tyr Val Thr Gly Ser Gly Leu Val His Arg Tyr Phe Leu 2580 2585 cca tcg cca tac ggc ctc gaa gat gca gcg tac ggg ggc agc ttc cac 7824 Pro Ser Pro Tyr Gly Leu Glu Asp Ala Ala Tyr Gly Gly Ser Phe His 2595 2600 acg ttc agg gag agc acg ccg ctg gga gtg gtg gtg cgg ggg gat gcc 7872 Thr Phe Arg Glu Ser Thr Pro Leu Gly Val Val Arg Gly Asp Ala 2610 2615 atg ttt gtg gcc ggg gac agt act gat tcc ata ttg aaa tat tcc ctq 7920

Met Phe Val Ala Gly Asp Ser Thr Asp Ser Ile Leu Lys Tyr Ser Leu

aac gca caa cct gtc ggc aac ata acc cat gcc gat acg cgc gcc ggq

2635

7968

2630

PCT/US99/22752

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| Asn | Ala | Gln | Pro | Val
264 | _ | Asn | Ile | Thr | His
265 | | Asp | Thr | Arg | Ala
265 | Gly
5 | |
|--|--|--|--|--|--|--|--|--|---|--|---|--|--|--|--|----------------------|
| | | | | Ala | | | | | Gly | | | | | Thr | cgc
Arg | 8016 |
| | | | Leu | | | | | Val | | | | | Val | | att
Ile | 8064 |
| | gta
Val
269 | Phe | | | | | Gly | | | | | Arg | | | tat
Tyr | 8112 |
| | | | | | | Leu | | | | | Asn | | | | aat
Asn
2720 | 8160 |
| | gtt
Val | | | | Val | | | | | Glu | | | | | Ser | 8208 |
| | cat
His | | | Pro | | | | | Ile | | | | | Pro | | 8256 |
| _ | aca
Thr | | _ | | _ | | | | | | | | | | | 8304 |
| | | 2755 | 5 | | | | 2760 |) | | | | 2765 | 5 | | | |
| | tcc
Ser
2770 | Gly
ggg | ggt | | | | tcg
Ser | gcc | | | | tcc
Ser | gga | | | 8352 |
| Leu | Ser
2770
gag
Glu | ggg
Gly
) | ggt
Gly
cgc | Asp
aga | ser
aac | Pro
2775
gcg
Ala | tcg
Ser | gcc
Ala
gac | Ser
agg | Asp | Ala
2780
ggc
Gly | tcc
Ser | gga
Gly
gaa | Val
gag | Val
cgc | 8352
8400 |
| gcc
Ala
2785 | Ser
2770
gag
Glu | ggg
Gly
agc
Ser | ggt
Gly
cgc
Arg | Asp
aga
Arg
gta | aac
Asn
2790
tcc
Ser | Pro
2775
gcg
Ala | tcg
Ser
gtg
Val | gcc
Ala
gac
Asp | Ser
agg
Arg | cct
Pro
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gac
Asp | Ala
2780
ggc
Gly
agg | tcc
Ser
gtg
Val | gga
Gly
gaa
Glu
gcc | Val
gag
Glu
gtc | cgc
Arg
2800
gac
Asp | |
| gcc
Ala
2785
ata
Ile | Ser
2770
gag
Glu
5 | ggg
Gly
agc
Ser
cat
His | ggt
Gly
cgc
Arg
ggt
Gly | aga
Arg
gta
Val
2805
acg
Thr | aac
Asn
2790
tcc
Ser | gcg
Ala
ctg
Leu | tcg
Ser
gtg
Val
gag
Glu | gcc
Ala
gac
Asp
gcg
Ala | agg
Arg
gcc
Ala
2810
gtg
Val | cct
Pro
2795
gac
Asp | Ala
2780
ggc
Gly
agg
Arg | tcc
Ser
gtg
Val
cct
Pro | gga
Gly
gaa
Glu
gcc
Ala | gag
Glu
gtc
Val
2815
ccg
Pro | cgc
Arg
2800
gac
Asp | 8400 |
| gcc
Ala
2785
ata
Ile
aac
Asn | gag
Glu
gga
Gly
atg | ggg
Gly
agc
Ser
cat
His
atg
Met | ggt
Gly
cgc
Arg
ggt
Gly
gat
Asp
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gcc
Ala | aga
Arg
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Val
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Thr | aac
Asn
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Ser
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Asp | gcg
Ala
ctg
Leu
agt
Ser | tcg
Ser
gtg
Val
gag
Glu
gcc
Ala | gcc
Ala
gac
Asp
gcg
Ala
ggc
Gly
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tcc
Ser | agg
Arg
gcc
Ala
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gtg
Val | cct
Pro
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gac
Asp
tac
Tyr | ggc
Gly
agg
Arg
gac
Asp | tcc
Ser
gtg
Val
cct
Pro | gga
Gly
gaa
Glu
gcc
Ala
agt
Ser
2830
gcc
Ala | gag
Glu
gtc
Val
2819
ccg
Pro | cgc
Arg
2800
gac
Asp
gac
Asp | 8400
8448 |
| gcc Ala 2785 ata Ile aac Asn gac Asp | gag
Glu
gga
Gly
atg
Met | ggg
Gly
agc
Ser
cat
His
atg
Met
ccc
Pro
2835 | ggt
Gly
cgc
Arg
ggt
Gly
gat
Asp
2820
gcc
Ala | aga
Arg
gta
Val
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acg
Thr | aac
Asn
2790
tcc
Ser
gat
Asp
tcc
Ser | gcg Ala ctg Leu agt Ser gac Asp | tcg
Ser
gtg
Val
gag
Glu
gcc
Ala
agg
Arg
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gac
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Ala
ggc
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Val
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Ala
atg | cct
Pro
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Tyr
ctg
Leu | ggc
Gly
agg
Arg
gac
Asp | tcc
Ser
gtg
Val
cct
Pro
cgc
Arg
ctt
Leu
2845 | gga
Gly
gaa
Glu
gcc
Ala
agt
Ser
2830
gcc
Ala | gag
Glu
gtc
Val
2815
ccg
Pro | cgc Arg 2800 gac Asp gac Asp atg Met | 8400
8448
8496 |

| | | | GJ y
ggg | | Ala | | | | | Asp | | | | _ | Asp | 8688 |
|-----|-----|-----|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| | | | gat
Asp
2900 | Thr | | | | | Val | | | | | Pro | | 8736 |
| | | | gcc
Ala
5 | | | | | Ser | | | | | Ala | | _ | 8784 |
| | | Asp | agg
Arg | | | | Asp | | | | | Thr | | | | 8832 |
| | Thr | | agg
Arg | | | Pro | | | | | Glu | | - | | _ | 8880 |
| | | | gcc
Ala | | Ser | | | | | Gly | | | | _ | Ser | 8928 |
| | | | ggt
Gly
2980 | His | | | | | Glu | | | | | Gly | | 8976 |
| | | | ggc
Gly | | _ | | - | Ile | _ | | _ | | Ser | | _ | 9024 |
| ` | | Ala | gcc
Ala | | | | Arg | | | | | Met | | | | 9072 |
| | Val | | gcg
Ala | | _ | Arg | | - | - | _ | Ala | | _ | | | 9120 |
| | | | gag
Glu | | Ser | | | Thr | | Pro | | | | | Met | 9168 |
| | | | aca
Thr
3060 | Val | | | Asp | | Ser | | | | | Ala | | 9216 |
| | | | Gly | | | Pro | | Phe | | | | | Arg | | | 9264 |
| | | Gly | gat
Asp | | | | | | | | | Val | | | | 9312 |
| cac | agt | ctg | gcc | cgg | gcc | gca | tcc | ata | tcc | gaa | ggc | gat | tcc | ccg | aca | 9360 |

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| | | | | | | | | | -36 | - | | | | | | |
|------------|--------------------|-----|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|-----------------|-------|
| His
310 | | Leu | Ala | Arg | Ala
311 | | Ser | Ile | Ser | Glu
311 | - | Asp | Ser | Pro | Thr
3120 | |
| | _ | | | _ | Arg | | - | | - | Gly | _ | | _ | | gtg
Val
5 | 9408 |
| _ | | | _ | Val | _ | | | | Leu | _ | _ | | | Leu | cag
Gln | 9456 |
| | cct
Pro | - | Ser | _ | | | | Asp | | | | | Asp | | _ | 9504 |
| | att
Ile
3170 | Ser | | - | | _ | Pro | - | | | _ | Val | | | | 9552 |
| - | ggc
Gly
5 | | | | | Gly | | | | _ | Gly | | _ | _ | | 9600 |
| | ggc
Gly | | | | Ile | | | | | Arg | | | | | Leu | 9648 |
| | ctc
Leu | | | Gly | | | | | Ala | | | | | Asp | | 9696 |
| | atc
Ile | _ | Pro | | | | | Glu | | | | | Ile | | _ | 9744 |
| | gag
Glu
3250 | Val | | | | | Pro | | | | | Ser | | | | 9792 |
| | aac
Asn | | | | | Leu | | | | | Cys | | | | | 9840 |
| | acc
Thr | | | | Tyr | | | | | Leu | | | | | Asp | 9888 |
| | ata
Ile | | | Val | | | | | Ala | | | | | Val | | 9936 |
| | ttg
Leu | | Gly | | | | | Thr | | | Val | | Leu | | | 9984 |
| | cac
His
3330 | Gly | | _ | _ | | Gln | | | _ | | Lys | | | | 10032 |

120

| ttg att ttg gac gcc gct gaa aac aga ccc ctg tca gtc tcg acg gac
Leu Ile Leu Asp Ala Ala Glu Asn Arg Pro Leu Ser Val Ser Thr Asp
3345 3350 3355 336 | |
|--|-------|
| ccc aag ccc gtg gag gat cca tcg ccc gtg cag cat ata gag tcc ctc
Pro Lys Pro Val Glu Asp Pro Ser Pro Val Gln His Ile Glu Ser Leu
3365 3370 3375 | 10128 |
| cag atg gat ccg gag ccc gtg gag tcc gag ccc ctc ccg atg gac tcc
Gln Met Asp Pro Glu Pro Val Glu Ser Glu Pro Leu Pro Met Asp Ser
3380 3385 3390 | 10176 |
| gag ccc gtg gag gat ctg gaa cct gtg cag cat cta gag tcc ctc ccg
Glu Pro Val Glu Asp Leu Glu Pro Val Gln His Leu Glu Ser Leu Pro
3395 3400 3405 | 10224 |
| atg gac ccc gag ccc gtg gag gat ctg gaa cct gtg cag cat ctc gag
Met Asp Pro Glu Pro Val Glu Asp Leu Glu Pro Val Gln His Leu Glu
3410 3415 3420 | 10272 |
| ccc gtg cag gga tcc ccg ccc gtg cag gga ggg ccg gag tcc gtg gagPro Val Gln Gly Ser Pro Pro Val Gln Gly Gly Pro Glu Ser Val Glu3425343034353440 | 10320 |
| tca ggc ata gca tac acg cta tgg cag ttc ctt tca gga ctg ctg gat
Ser Gly Ile Ala Tyr Thr Leu Trp Gln Phe Leu Ser Gly Leu Leu Asp
3445 3450 3455 | 10368 |
| gcc ctg ggt ctt gcc gac ccg gat gtc gga tct gtc caa aaa acg tcc
Ala Leu Gly Leu Ala Asp Pro Asp Val Gly Ser Val Gln Lys Thr Ser
3460 3465 3470 | 10416 |
| tga
* | 10419 |
| <210> 4 <211> 3472 <212> PRT <213> Cenarchaeum symbiosum | |
| • | |
| <pre><400> 4 Met Pro Ala Pro Pro Gly Glu Gly Ser Leu Gly Gly Val Ala Ile Ser 1 5 10 15</pre> | |
| Asp Asp Gly Arg Tyr Met Tyr Ala Ile Gly Arg Asp Leu Leu Thr Val
20 25 30 | |
| Tyr Arg Tyr Thr Met Asn Pro Pro His Asp Ile Ala Ser Ala Ala Leu 35 40 45 | |
| Gly Ala Gln Ser Phe Ser Leu Pro Gly Gly Ile Ser Pro Ala Pro Gly 50 55 60 | |
| Ala Pro Thr Gly Leu Asp Ile Ser Asp Asp Gly Arg His Leu Tyr Val | |
| 65 70 75 80 Pro Asp Glu Asn Gly Val Val Tyr Arg Phe Asp Leu Glu Ser Pro Tyr 85 90 95 | |
| Arg Leu Asp Gly Gly Thr Phe Gly Ser Ser Val Tyr Val Gly Ser Asp | |
| Val Ala Ala Pro Arg Gly Val Tyr Val Ala Pro Gly Gly Ser Leu Met 115 120 125 | |

Leu Val Ser Asp Ser Ala Asp Gly Thr Ile His Arg Tyr Glu Leu Ala Ser Pro Tyr Glu Pro Ala Gly Ala Ala Asn Arg Gly Ser Phe Asp Val 150 155 Ser Asp Met Asp Gly Ser Pro Val Gly Ala Gly Phe Ala Gly Gly Leu 165 170 His Met Tyr Val Ala Gly Asn Asp Thr Gly Arg Val Tyr Gln Tyr Pro 185 Ala Gly Thr His Gln Ile Gln Glu Ala Ala Gly Pro Arg Leu Leu 200 205 Ser Ala Val Leu Asp Lys Asp Gly Thr Leu Arg Ala Ala Phe Asp Gly 215 Thr Val Asp Ala Gly Ser Val Gln Pro Gly Met Ile Thr Ile Arg Asp 235 Gly His Gly Ser Asn Thr Gly Ile Pro Leu Leu Leu Ala Gly Gly Ala 250 Ala Asp Ser Asp Val Met Thr Phe Val Val Pro Glu Lys Asp Arg Ala 265 260 Glu Ala Ala Ala Tyr Gly Asp Gln Ser Leu His Val Pro Ala Ala Ala 280 Leu Ala Gly Thr Gly Gly Gly Pro Phe Val Pro Asp Phe Ser Gly Gly 295 Ser Leu Leu Ala Ser Leu Tyr Arg His Glu Arg Pro Phe Gln Gly Glu 310 315 Glu Met Ala Arg Thr Glu Arg Ser Asp Arg Tyr Ala Leu Thr Val Thr 325 330 Ala Gly Gly Ser Gln Met His Val Gly Gly Ala Gly Gly Asn Ile Thr 345 Trp Tyr Asp Leu Gly Thr Pro His Asp Ile Thr Thr Gly Val Arg Ala 360 Gly Ser Asp Ile Leu Pro Ala Tyr Pro Ser Ala Gly Arg Asn Val Val 375 Pro Ser Ile Thr Gly Ile Ala Phe Ser Asp Asp Gly Met Arg Leu Phe 390 395 Ala Ala Asn Arg Gly Asp Arg Ile Pro Met Tyr Gln Leu Asp Ser Pro 405 410 Tyr Asp Ile Gly Ser Ala Ser Leu Glu Gly Thr Leu Phe Thr Gly Phe 425 Gln Ser Gly Ile Ala Phe Ser Asp Asp Gly Thr Arg Met Phe Ala Ala 440 Leu Leu Thr Glu Asn Ala Ile Arg Gln Tyr Asp Leu Glu Gly Pro Tyr 455 460 Asp Ile Arg Gly Ala Gly Asn Ala Gly Gln Tyr Asp Leu Asp Ile Pro 470 475 Leu His Pro Gly Leu Leu Phe Leu Leu Thr Ser Gly Val His Phe Ser 485 490 Pro Asp Gly Thr Arg Met Phe Val Gly Glu Gly Ile Ser Asp Ala Glu 505 Asp Ala Asn Ala Asn Arg Asp Val Asn Val Asn Leu Trp His Arg Phe 520 525 Asp Leu Ser Thr Pro Phe Asp Val Leu Thr Ala Glu Arg Val Asp Thr 535 540 Tyr Glu Tyr Ser Thr Gly Pro Ala Gly Asp Leu Glu Asp Leu Ser Leu 555 Ser Pro Asp Gly Arg Arg Leu Tyr Thr Leu Ser Ser Glu Arg Val Ser 570 565 Ser Ser Glu Tyr Thr Ile Thr Arg Ala Gln Tyr Trp Leu Pro Glu Pro 585

Tyr Asp Val Thr Pro Pro Tyr His Val Pro Ser Phe Asn Ala Ser Gln Gly Gly Asn Leu Ala Asp Pro Tyr Gly Met Ala Phe Ser Pro Asp Gly 615 620 Thr Arg Leu Leu Val Thr Gly His Gly Gln Thr Asn Ala Lys Leu Phe 635 630 His Leu Asn Pro Pro Phe Asp Val Gly Thr Ala Val Phe His Asp His 650 Gly Arg Phe Arg Pro Gly Gly Pro Ala Ser Glu Ile Glu Ala Ser Gly 665 Ile Ser Leu Ser Ala Asp Gly Ser Arg Met Phe Leu Ser Asp Arg Gly 680 Arg Gly Ala Ile Ser Gln Tyr Thr Leu Val Ala Pro Phe Asp Val Glu 700 695 Phe Ala Ser Asp Val Ser Ala Asp Gly Gln Leu Asp Val Gly Ala Gln 710 715 Asp Ala Leu Pro Gly Gly Leu Ala Phe Ser Pro Gly Gly Thr Arg Leu 725 730 Phe Met Val Gly Gly Met Asp Arg Ser Val His Met Tyr Ser Leu Asn 745 Thr Pro Phe Asp Leu Gly Gly Ala Glu His Ala Ala Ser Phe Gly Val 760 Gly Asp Arg Val Ser Asp Pro Leu Gly Ile Ala Phe Gly Asn Gly Gly 775 780 Thr Lys Met Leu Ile Ala Asp Thr Thr Gly Phe Val His Gly Tyr Asp 790 795 Leu Gly Ala Pro Tyr Asp Ile Ser Gly Pro Ala Tyr Ser Gly Ile Phe 810 Asp Ala Gly Gly Ser Ile Arg Asp Val Ala Val Gly Gly Ser Met 825 Phe Ile Leu Glu Gly Glu Thr Asp Arg Val Tyr Glu His Arg Pro Gly 840 Ile Tyr Pro Val Val Ser Ala Leu Asp Gly Pro Ala Leu Val Ser Ala 855 860 Ala Ala Asp Ala Arg Val Gly Ala Ala Glu Val Leu Phe Asp Arg Ala 870 875 Val Asp Val Gly Gly Ile Asp Pro Gly Gly Val Arg Ile Val Asp Ala 885 890 Ala Gly Pro Leu Pro Gly Val Val Ile Ser Asp Ala Val Ile Pro Gly 905 Glu Asp Pro Gly Val Ala Arg Phe Ser Leu Ser Asp Ala Glu Val Leu 920 925 Ala Val Ser Gly Tyr Ala Glu Pro Ser Leu Val Phe Gly Arg His Ala 935 Val Pro Gly Ala Ala Gly Gly Thr Phe Pro Ser Gln Ile Gly Asn Ala 955 950 Thr Glu Leu Val Gly Ser Ile Pro Asn Pro Thr Leu Asp Phe Gly Thr 970 Thr Leu Thr Gly Ala Ala Phe Ser Ala Asp Gly Thr Val Val Phe Leu 980 985 Ser Asp Gly Pro Thr Gly Arg Val Tyr Pro Tyr Ser Leu Asn Ile Pro 1000 1005 Phe Asp Ile Ser Ser Ala Ala Pro Gly Gly Phe Val Ile Val Pro Val 1015 1020 Gly Val Ser Asp Ile Ala Phe Ser Ala Asp Gly Arg Asn Met Leu Val 1030 1035 Ala Asp Glu Thr Gly Gly Ile His Arg Tyr Leu Ala Arg Ser Pro Tyr 1045 1050

| Glu | Ile | Gly | Thr | _ | Phe | Ile | Lys | Ser
106 | | Leu | Gly | Glu | Phe | | Glu |
|---------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|
| Thr | Phe | Ser
107 | Ala | | Pro | Arg | Val | Gln | | Leu | Ala | Gly
108 | Ile | - | Phe |
| Ser | His
109 | qaA | _ | Met | Ile | Met
109 | Leu | | Ala | Gly | Gly
110 | Ser | | Ser | Val |
| His
110 | Arg | | Ser | Leu | Pro | Ser | | Tyr | Ala | Val | | Gly | Ala | Lys | Tyr
1120 |
| | | Thr | Ala | Met
112 | Ile | | Gly | Ser | Pro | Ser | | Leu | Glu | Phe | |
| Ser | qaA | Gly | Leu
114 | _ | Met | Phe | Val | Pro
114 | | Ala | Gly | Ser | Glu
115 | | Ala |
| Ala | Val | Tyr | Gly | | Ala | Ala | Pro | _ | Gly | Ile | Gly | Glu
116 | Ala | | Pro |
| Leu | Pro | Pro | | Phe | Leu | Gly
1179 | Val | | Ala | Glu | Glu
1180 | Ala | | Leu | Ser |
| | Asp | | Arg | His | | Leu | | Pro | Gly | Arg | Pro | | Leu | Ser | |
| 1185
Tyr | | Leu | Phe | Ser | 1190
Thr | | Leu | Glu | Leu | 1199
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| - | | | | 120 | | | | | 121 | _ | | | | 121! | _ |
| Ile | Asp | Gly | Gly
1220 | | Cys | Glu | Asp | Gly
122 | | Tyr | Ala | Phe | Glu
123 | | Pro |
| Gly | Arg | Gly
1235 | | Gly | Val | Ser | Leu
1240 | | Ala | Ser | Ile | Thr
1245 | | Ala | Asp |
| Gly | Pro
1250 | Gly | | Gly | Glu | Leu
1255 | His | | Phe | Ala | Gly
1260 | Pro | | Met | Pro |
| Ala | | | Met | Glu | Gln | | | Leu | Asp | Ser | | | Glv | Thr | Leu |
| 1265 | ; | | | | 1270 |) | | | | 1275 | 5 | | _ | | 1280 |
| Arg | Val | Arg | Leu | Asp
1289 | _ | Thr | Val | qaA | Val
129 | qaA
O | Thr | Val | Arg | Pro
1295 | - |
| Lys | Met | _ | Val
1300 | | Asp | Ser | Asp | Gly
1309 | | Gln | Thr | Thr | Leu
1310 | | Asn |
| Ser | | Leu
1315 | | Asn | Ala | Glu | Asn
1320 | | Asn | Ile | Leu | Leu
1325 | | Arg | Leu |
| Asp | Asp
1330 | | Ala | Ala | Gly | Lys
1335 | | Ser | Gly | Tyr | Thr
1340 | | Pro | Val | Phe |
| _ | Thr | | Ser | Ser | | Phe | | Gly | Thr | Asp | Gly | | Thr | Arg | |
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| Ser | Glv | Asp | | | | Pro | | | | Glu | Phe | Ser | | | |
| | • | | 1380 | | | | | 1385 | | | | | 1390 | _ | |
| Met | | Met
1395 | | Val | Thr | Gly | Ile
1400 | | Thr | Pro | Gly | Ile
1405 | | Ile | Phe |
| | Leu
1410 | | Ala | Pro | Phe | Asp
1415 | | Thr | Leu | Pro | Lys
1420 | | Ser | Gly | Ser |
| Thr | Asn | Ile | Gly | Gly | Leu | Ser | Val | Ser | Asp | Leu | Ala | Phe | Ala | Asn | Asn |
| 1425 | | | | | 1430 | | | | | 1435 | | | | | 1440 |
| _ | | | | 1445 | I | | | | 1450 | | | | _ | 1455 | i - |
| Ala | Leu | _ | Asp
1460 | _ | Tyr | Asn | | Val
1465 | | Gly | Thr | Thr | Gln
1470 | - | Phe |
| Arg | | Thr : | Leu | Asp | Thr | | Gln
1480 | _ | Ile | Pro | | Ser
1485 | | Tyr | Thr |
| Ser | | | Gly | Leu | Ser | | | | Ala | Tyr | | | | Ile | Asp |
| | 1490 | _ | _ | | | 1495 | | | | _ | 1500 | _ | - | | _ |
| Leu
1505 | | Val : | Leu | | | Pro . | | | | Ser | | Thr | Thr | | Ile |

| Ile | Pro | Tyr | Ser | Leu
152 | | Arg | Pro | Asp | | | Thr | Gly | Met | _ | Phe |
|--|---|---|--|--|---|---|---|---|--|---|---|--|--|---|--|
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| Thr | Pro | Asp | 154 | _ | Arg | met | Pne | | ser
5 | | GIU | Asn | 155 | | Asp |
| Gln | Tyr | Leu | Leu | Ser | Glu | Pro | Phe | Ala | Val | Thr | Thr | Ser | Val | Phe | Leu |
| | | 155 | 5 | | | | 156 | 0 | | | | 156 | 5 | | |
| Arg | Thr
1570 | | Pro | Ile | Asp | Gly
157 | | Ala | Glu | Gly | Ile
158 | _ | Phe | Val | Asp |
| Asn | Glv | Ara | Glv | Leu | Phe | Val | Pro | Glv | Ala | Asp | Glv | Tle | Tle | Gln | Arg |
| 158 | _ | 5 | , | | 159 | | | , | | 159 | | | | 01 | 1600 |
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| GIA | GIU | | | Leu | Ala | GLA | | | Asn | Ala | Ser | _ | Asn | Val | Gln |
| | | 1635 | | | | | 1640 | | | | | 164 | | | |
| Ser | Pro | Ser | Gly | Ile | Glu | Phe | Ser | Gly | Asp | Gly | Thr | Gly | Met | Phe | Val |
| | 1650 | | | | | 1655 | | | | | 1660 | | | | |
| Thr | Gly | Phe | Gly | Ala | Ala | Gly | Val | Asn | Glu | Phe | Ser | Leu | Ser | Ala | Pro |
| 1669 | 5 | | | | 1670 |) | | | | 1675 | 5 | | | | 1680 |
| Phe | Asp | Thr | Thr | Leu | Pro | Val | His | Val | Glu | Leu | His | Asp | Ile | Gly | Gly |
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| Gln | Pro | Ala | Val | Asp | Leu | Ala | Phe | Ala | Glu | Asp | Glv | Ara | Thr | Leu | Leu |
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| Leu | Leu | Ala | - | | Glv | Thr | T.e.u | | | Tvr | Ser | T.em | Ala | | Acn |
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Pro | Thr Trp Ile Asp 1835 Leu Tyr | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val | 1760
Val
Pro
Thr
Arg
Met
1840
Gly
Asn |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val | Pro
1785
Gly
Leu
Pro
Leu
Asp
1865
Asp | Arg
1770
Leu
Arg
Ser
Val
Phe
1850
Pro | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val | Pro
1785
Gly
Leu
Pro
Leu
Asp
1865
Asp | Arg
1770
Leu
Arg
Ser
Val
Phe
1850
Pro | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val | Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser | Arg 1770 Leu Arg Ser Val Phe 1850 Pro Gly Tyr | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val | Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser | Arg 1770 Leu Arg Ser Val Phe 1850 Pro Gly Tyr | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val | Gly Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp | Arg 1770 Leu Arg Ser Val Phe 1850 Pro Gly Tyr | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 Tyr |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 Asp | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp Ser | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser | Ala 1765 Phe Phe Asp Thr Asn 1845 Tyr Glu Lys Arg His 1925 | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp Tyr Asp 1800 Leu Ile Ala Glu Phe 1880 Val Ala Val | Gly Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp | Arg 1770 Leu Arg Ser Val Phe 1850 Pro Gly Tyr Thr Met | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp Gly | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile Asn | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro | Val
1775
Thr
Ser
Val
Gly
Val
Pro
Gln
Leu
1935 | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 Tyr |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 Asp | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp Ser Pro | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser | Ala 1765 Phe Phe Asp Thr Asn 1845 Tyr Glu Lys Arg His 1925 | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg | Asp Tyr Asp 1800 Leu Ile Ala Glu Phe 1880 Val Ala Val | Gly Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp | Arg
1770
Leu
Arg
Ser
Val
Phe
1850
Pro
Gly
Tyr
Thr
Met
1930
Asp | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp Gly | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile Asn His | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro
Gln
Leu
1935 | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 Tyr |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 Asp | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val Ser Thr | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp Ser Pro | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser Arg | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys
Arg
His
1925
Val | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg Ala Gly | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val
Ala
Val | Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp | Arg
1770
Leu
Arg
Ser
Val
Phe
1850
Pro
Gly
Tyr
Thr
Met
1930
Asp | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 Pro | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp Gly Ile | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile Asn His | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro His Ser 1950 | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro
Gln
Leu
1935 | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 Tyr |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 Asp | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val Ser Thr | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp Ser Pro | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser Arg | Ala
1765
Phe
Phe
Asp
Thr
Asn
1845
Tyr
Glu
Lys
Arg
His
1925
Val | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg Ala Gly Ser | Asp
Tyr
Asp
1800
Leu
Ile
Ala
Glu
Phe
1880
Val
Ala
Val | Gly Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp Ser Asp | Arg
1770
Leu
Arg
Ser
Val
Phe
1850
Pro
Gly
Tyr
Thr
Met
1930
Asp | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 Pro | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp Gly Ile | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile Asn His | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro His | Val
1775
Thr
Ser
Val
Gly
Glu
1855
Gly
Val
Pro
Gln
Leu
1935 | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe Ile 1920 Tyr |
| 1745 Ser Ile Thr Glu Ser 1825 Gln Leu Thr Glu Asp 1905 Asp Ile | Ser Pro Gly Asn 1810 Leu Phe Ile Ile Tyr 1890 Val Ser Thr | Ile Phe Ile 1795 Gly Thr Ala Tyr Ser 1875 Asp Ser Pro Asn Asn | Ile Glu 1780 Asp Ile Tyr Asp Asn 1860 Val Thr Ser Arg Ser 1940 Asn | Ala 1765 Phe Phe Asp Thr Asn 1845 Tyr Glu Lys Arg His 1925 Val | Ala Val Ala Gln Gly 1830 Gly Asp Phe Arg Thr 1910 Val Phe | Phe Ser Pro Tyr 1815 Thr Arg Leu Ser Val 1895 Arg Ala Gly Ser | Asp Tyr Asp 1800 Leu Ile Ala Glu Phe 1880 Val Ala Val Glu Ser 1960 | Gly Pro 1785 Gly Leu Pro Leu Asp 1865 Asp Ser Asp 1945 Ala | Arg
1770
Leu
Ser
Val
Phe
1850
Pro
Gly
Tyr
Thr
Met
1930
Asp | Thr Trp Ile Asp 1835 Leu Tyr Ser Glu Leu 1915 Pro Thr | Asp Arg Met Pro 1820 Gly Ala Ala Val Leu 1900 Asp Gly Ile | Gln Pro Phe 1805 Phe Val Asp Leu Met 1885 Glu Ile Asn His Gly 1965 | Tyr Gly 1790 Leu Asp Glu Ser Asp 1870 Tyr Phe Pro His Ser 1950 | Val
1775
Thr
Ser
Val
Glu
1855
Gly
Val
Pro
Gln
Leu
1935
Tyr | 1760 Val Pro Thr Arg Met 1840 Gly Asn Leu Phe 1920 Tyr Gly Gly |

| Arg
198 | | : Phe | : Lei | ı Ile | Gly
199 | | / Asr | ı Gly | / Phe | Asp
199 | | Glr | val | . Ile | His
2000 |
|------------|------------|-------|-------|--------|------------|-------------------|-------|-------|------------|------------|--------|------|------|-------|-------------|
| Asp | Tyr | Met | Lei | ı Glv | Thr | Arc | ı Tvı | Asc | Ile | Ser | Sei | Arc | Ser | Lev | Leu |
| - | • | | | 200 | | | 1- | | 201 | | | | , | 201 | |
| Àsp | Thr | Tvr | Ala | | | Gla | , Pro | Val | | | Pro | Δla | Glu | | Asp |
| • | | -3 | 202 | | | , | | 202 | | | | | 203 | | · wop |
| Phe | Ser | • Phe | | | T.e.i | Q _D | - Met | | | Tle | Car | The | | - | Ser |
| | | 203 | | , ,,,, | | | 204 | | | | | 204 | | СТУ | SEL |
| Val | Т | | | . 61. | . 1 | 7 ~~ | | | Dho | T1. | . 17-1 | | | | • |
| val | 205 | | ıyı | СТУ | Den | . AS _P | | PIC | Pile | TIE | | | Int | met | Asp |
| TT: | | | | | | | _ | | 5 | • | 206 | | _ | _ | _ |
| | | GIU | Ser | Pne | | | Pro | vai | Pro | | | Ala | Asp | Asn | Ser |
| 206 | | | | | 207 | | | | | 207 | | | | | 2080 |
| Ile | Ser | Asp | Leu | | | Gly | Ser | Ser | | | Asn | Ala | Val | | Ser |
| | | | | 208 | | | | | 209 | | | | | 209 | - |
| His | Glu | Gly | | | Thr | Leu | Tyr | | | Val | Leu | Asp | Ile | Pro | Tyr |
| | | | 210 | | | | | 210 | | | | | 211 | | |
| Gly | Ala | | | Asp | Ile | Asp | Arg | Leu | Glu | Leu | Pro | Leu | Val | Gly | Val |
| | | 211 | | | | | 212 | - | | | | 212 | | | |
| Pro | | | Phe | Glu | Phe | Ser | Asp | Asn | Gly | Arg | Gln | Leu | Tyr | Ile | Gly |
| | 213 | | | | | 213 | | | | | 214 | | | | |
| Ala | Phe | Arg | Asp | Ser | Gln | Ser | Ser | Pro | Gly | Thr | Leu | Pro | Ala | Gly | Leu |
| 214 | 5 | | | | 215 | 0 | | | | 215 | 5 | | | | 2160 |
| Gln | Arg | Tyr | Glu | Leu | Gly | Ile | Pro | Tyr | Asp | Leu | Ala | Ser | Ala | Val | Phe |
| | | | | 216 | 5 | | | | 217 | 0 | | | | 217 | 5 |
| Ala | Gln | Ser | Leu | Gly | Ile | Phe | Asp | Phe | Pro | Pro | Phe | Asn | Gly | Met | Arg |
| | | | 218 | | | | _ | 218 | | | | | 219 | | |
| Ala | Asn | Gly | Ser | Leu | Ala | Gly | Leu | His | Val | Pro | Pro | asA | | | Ile |
| | | 219 | | | | • | 220 | | | | | 220 | _ | | |
| Leu | Phe | Arq | Ala | Glv | Asn | Ala | Glu | Arq | Thr | Val | Ile | | | Asp | Met |
| | 221 | | | • | | 221 | | • | | | 222 | | -2- | | |
| Asp | Ser | His | Asp | Leu | Asp | | Leu | Ser | Phe | Ara | | | Phe | Lvs | Pro |
| 2225 | | | • | | 2230 | | | | | 223 | | | | -,- | 2240 |
| Asp | Val | Glv | Gln | Ser | | | Asn | Ile | Ara | | | Asp | Tle | Ser | |
| _ | | | | 224! | | | | | 2250 | | | 1100 | | 225 | |
| Asp | Glv | Met | Phe | | | Leu | Leu | Gln | | | Val | T.eu | Δen | | |
| | , | | 226 | | -1- | | | 226 | | | ••• | шси | 2270 | | - y - |
| Asn | Len | Thr | | | Tur | Ser | Leu | | | Dro | בומ | Tur | | | The |
| | Deu | 2275 | | DCI | LYL | Jer | 2280 | | AIG | FIU | AIA | 2285 | | GIY | Int |
| I.a.ı | Aan | | | Dro | G1 | 7.00 | Val | | Dro | λ | C1 | | | Db - | 0 |
| Deu | 2290 | | GIU | PLO | GIU | 229 | | 116 | PLO | ALG | _ | | ser | Pne | ser |
| Ara | | | Th~ | Co. | T 0 | | Met | mh | <i>α</i> 1 | αī | 2300 | | | ••• | |
| 2305 | | GIY | TILL | 261 | 2310 | | mec | TIIL | GIA | | - | vai | Asp | HIS | |
| | | Ф | 81.0 | T | | | D | m | 3 | 2315 | | | | | 2320 |
| urs | GIU | Tyr | Ala | | | GIU | Pro | Trp | | | Arg | Asn | Ala | | |
| n1 - | ~ 3 | | _ | 2325 | | _ | - • | | 2330 | | | | | 2335 | |
| Ala | GIY | ser | | | Ile | Ser | Ala | | | Gly | Ala | Pro | _ | - | Leu |
| | _ | | 2340 | | | | | 2345 | | | | | 2350 | | |
| Asp | Ile | | | Asp | Gly | Thr | Thr | | His | Thr | Met | | | Arg | Asp |
| | | 2355 | | | | | 2360 | | | | | 2365 | | | |
| Phe | Asp | Thr | Gly | Pro | Ala | Ser | Leu | Val | Asn | His | Ile | Leu | Pro | Gly | Gln |
| | 2370 |) | | | | 2375 | 5 | | | | 2380 |) | | | |
| Tyr | Ser | Leu | Leu | Thr | Asp | Ala | Pro | Ala | Phe | Ala | Tyr | Pro | Val | Glu | Glu |
| 2385 | | | | | 2390 | | | | | 2395 | | | | | 2400 |
| Glu | Gly | Ala | Pro | Gly | Asp | Leu | Ala | Phe | Ser | Asp | Asp | Gly | Met | Ara | |
| | - | | | 2405 | | | | | 2410 | | • | - | | 2415 | |
| Phe | Val | Ala | Gly | Val | Asn | Asn | His | Leu | | | Tyr | Asn | | | |
| | | | 2420 | | | | | 2425 | | | | | 2430 | | - |
| Pro | Tyr | Asp | | | Asn | Ala | | | | Ile | Ser | | | | Leu |
| | | 2435 | | | | | 2440 | | | | | 2445 | - | | |

| Tnr | | _ | Arg | GIA | Pro | | - | Let | vaı | . Pne | | - | GIU | ı Asn | Asp |
|-------------|-------------|-------------|-------------|-------------|-------------|------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|----------------|
| Dhe | 245 | | ጥኮል | · Glv | - הות | 245 | | . G) = | Dhe | . Val | 246 | | n Phe | The | The |
| 246 | | 361 | 1111 | GLy | 247 | | , Alc | GII | | 247 | _ | GII | i Pile | | 248 |
| | | Pro | Tvr | Asp | | - | Thr | : Ile | Thr | | | Ast |) Asn | Glv | |
| | 3 | | -1 | 248 | | | | | 249 | | | | | 249 | |
| Tvr | Lvs | Val | Ser | | | Gly | . Lev | Pro | | | Ile | Arc | Phe | | |
| - | - | | 250 | | - | - | | 250 | | • | | _ | 251 | | |
| Asp | Gly | Met | Lys | Met | Phe | Ile | Ser | Gly | Gln | Glu | Thr | Ala | Met | Ile | Tyr |
| | | 251 | 5 | | | | 252 | 0 | | | | 252 | .5 | | |
| Gln | Tyr
253 | | Leu | Pro | Ser | Pro
253 | | Asp | Thr | Ser | Gly
254 | | Val | Arg | Asp |
| Arg
254 | | Glu | Ile | Val | Ala
255 | _ | Leu | Phe | Arg | Asn
255 | | Gly | Leu | Ser | Val
256 |
| Gly | Leu | Asn | Glu | Pro | Ser | Pro | Ser | Gly | Phe | Asp | Phe | Ser | Glu | Asp | Gly |
| | | | | 256 | 5 | | | | 257 | 0 | | | | 257 | 5 |
| Met | Glu | Leu | Tyr
258 | | Thr | Gly | Ser | Gly
258 | | Val | His | Arg | Tyr
259 | | Leu |
| Pro | Ser | Pro | Tyr | Gly | Leu | Glu | Asp | Ala | Ala | Tyr | Gly | Gly | Ser | Phe | His |
| | _ | 259 | | | | | 260 | | | _ | | 260 | | | |
| | 261 | 0 | | | | 261 | 5 | | | | 262 | 0 | Gly | - | |
| Met
262 | | Val | Ala | Gly | Asp
2630 | | Thr | Asp | Ser | Ile
263 | | Lys | Tyr | Ser | Leu
2640 |
| Asn | Ala | Gln | Pro | Val
264 | | Asn | Ile | Thr | His
265 | | Asp | Thr | Arg | Ala
265 | Gly |
| Ile | Ala | Asp | Arg | | | Ile | Val | Phe | | - | Met. | Ala | Asp | | |
| | | | 266 | | | | | 266 | | | | | 2670 | | 5 |
| Ala | Glu | Ile
267 | | Asp | Gly | Ala | Asp
268 | | Val | His | Lys | Ser
268 | Val
5 | Lys | Ile |
| Asp | Val
2690 | | Pro | Ile | Ser | Glu
269 | | Ile | Thr | Val | Gly
2700 | - | Ala | Leu | Tyr |
| Pro | Glu | Asp | Ala | Ala | Ile | Leu | Asp | Asp | Gly | Ala | Asn | Ala | Thr | His | Asn |
| 2709 | 5 | _ | | | 2710 |) | | _ | _ | 2715 | 5 | | | | 2720 |
| Arg | Val | Val | Ile | Ile
2729 | | His | Asp | Ile | Thr
2730 | | Gly | Asp | Ala | Pro
2739 | |
| Ile | His | Asp | Glu | Pro | Ile | Ala | Val | Gly | Ile | Tyr | Ala | Leu | Gly | Pro | Met |
| | | | 2740 | | | | | 2745 | - | | | | 2750 | - | |
| Asp | Thr | | | Val | Val | Asp | | | Arg | Leu | Ala | | Ser | Ala | Ser |
| _ | _ | 2759 | | _ | _ | _ | 2760 | _ | _ | _ | | 276 | | | _ |
| | 2770 |) | | | | 277 | 5 | | | | 2780 |) | Gly | | |
| Ala
2785 | | Ser | Arg | Arg | Asn
2790 | | Val | Asp | Arg | Pro
2795 | | Val | Glu | Glu | Arg
2800 |
| Ile | Gly | His | Gly | | | Leu | Glu | Ala | | | Arg | Pro | Ala | Val | Asp |
| | | | | 2805 | | | | | 2810 | | | | | 2815 | |
| | | | 2820 |) | | | | 2825 | i | | | _ | Ser
2830 |) | _ _ |
| Asp | Gly | Pro
2835 | | Val | Ser | Asp | Arg
2840 | | Ala | Leu | Gly | Leu
2845 | Ala | Arg | Met |
| Ala | Ala | Asp | Arg | Pro | Ala | Val | Asp | Asp | Met | Met | Asp | Thr | Asp | Ser | Ala |
| | 2850 |) | | | | 2859 | 5 | | | | 2860 |) | _ | | |
| Gly | Val | Tyr | Asp | Arg | | | Asp | Asp | Gly | Pro | Ala | Ile | Ser | Asp | Arg |
| 2865 | | | | _ | 2870 | | . 0 | | - | 2875 | | | | | 2880 |
| | | | | 2885 | | | | | 2890 |) | | | Ala | 2895 | ; |
| Asp | Met | | Asp
2900 | | Gly | Ser | | Gly
2905 | | Tyr | Asp | _ | Ser
2910 | | Asp |

Asp Gly Pro Ala Ile Ser Asp Arg Ser Ala Leu Gly Leu Ala Arg Met 2920 Ala Ala Asp Arg Pro Ala Val Asp Asp Met Met Asp Thr Gly Ser Glu 2935 2940 Ser Thr Ser Arg Leu Gly Pro Val Asp Arg Pro Glu Ile Val Glu Arg 2950 2955 His Ser Leu Ala Ala Ser Val Tyr Leu Ser Gly Gly Asp Ser Pro Ser 2965 2970 Val Ala Asp Gly His Asp Val Glu Ser Glu Gly Arg Arg Asp Gly Gly 2980 2985 Asp Arg Pro Gly Ile Asp Glu Arg Ile Val Ile Lys Ile Ser Tyr Ser 3000 Arg Gly Ala Ala Asp Ala Pro Arg Val Glu Asp Ala Met Glu Thr Ser 3010 3015 3020 Gly Val Thr Ala Tyr Ser Arg Gly Ala Ala Asp Ala Pro Arg Val Glu 3030 3035 Asp Ala Met Glu Thr Ser Gly Val Thr Val Pro Arg Arg Ser Thr Met 3050 3045 Asp Ala Pro Thr Val Ala Asp Asp His Ser Leu Ala Arg Thr Ala Ser 3060 3065 Ile Ser Glu Gly Asp Ser Pro Thr Phe Ala Glu Ala Arg Arg Ala Asp 3075 3080 3085 Thr Val Gly Asp Ile Asp Glu Val Asp Ala Pro Thr Val Ala Asp Asp 3090 3095 3100 His Ser Leu Ala Arg Ala Ala Ser Ile Ser Glu Gly Asp Ser Pro Thr 3115 3110 Phe Ala Glu Val Arg Arg Ala Asp Thr Val Gly Asp Ile Asp Glu Val 3125 3130 Asp Ala Pro Ala Val Ala Glu Arg Leu Leu Ala Val Leu Gly Leu Gln 3140 3145 3150 Ala Pro Asp Ser Pro Gly Val Trp Asp Thr Val Gly Ile Asp His Ser 3160 3155 Glu Ile Ser Gly Asp Pro Val Pro Glu Pro Arg Val Val Pro Arg Gly 3175 3180 Gly Gly Gly Gly Gly Gly Ser Ser Asn Arg Gly Leu Glu Pro His 3190 3195 Gly Gly Gly Tyr Glu Ile Asp Phe Glu Phe Arg Ile Asp Gly Arg Leu 3205 3210 Val Leu Phe Asn Gly Thr Asp Val Leu Ala Glu Ser Gly Lys Asp Leu 3225 Leu Ile Arg Pro Val Phe Arg Pro Glu Gly Ser Phe Asn Ile Phe Asp 3235 3240 3245 Met Glu Val Leu Phe Thr Ala Pro Gly Gly Glu Ile Ser Thr Ala Tyr 3255 Tyr Asn Arg Ala Gly Ile Leu Met Gly Ile Asp Cys Gly Glu Leu Ile 3270 3275 Met Thr Asp Thr Thr Tyr Ser Cys Asp Met Leu Asp Ile Phe Gly Asp 3290 3285 Glu Ile Tyr His Val Glu Arg Leu Asp Ala Phe Asn Gly Met Val Ile 3300 3305 Ser Leu Asp Gly Pro Leu Asp Gly Thr Val Ser Val Ser Leu Arg Asp 3315 3320 3325 Asn His Gly Ile Pro Leu Ala Gln His Arg Leu His Lys Tyr Glu Ile 3335 3340 Leu Ile Leu Asp Ala Ala Glu Asn Arg Pro Leu Ser Val Ser Thr Asp 3355 3350 Pro Lys Pro Val Glu Asp Pro Ser Pro Val Gln His Ile Glu Ser Leu 3365 3370

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| 61 | - 14-4 | | | - 01. | . D | | 61. | | | | | . Des | | | | |
|-----------|-------------|------------|-----------|----------|-------|-----|------------|-----------|-----------|-----|-------|------------|------------|-----------|-------|-----|
| GI | п ме | . ASI | 338 | | ı Pro | vai | . GIU | 338 | | Pro | . rec | Pro | мет
339 | _ | Ser | |
| Gl | u Pro | | | ı Asp | Leu | Glu | Pro
340 | | Gln | His | Leu | | | Leu | Pro | |
| Me | t Ası | 339
Pro | | ı Pro | Val | Glu | | | . Glu | Pro | Val | 340
Glr | | Leu | Glu | |
| | 343 | LO | | | | 341 | 5 | | | | 342 | 0 | | | | |
| | | Glr | Gly | Ser | | | Val | Gln | Gly | _ | | Glu | Ser | Val | Glu | |
| 34
Se | 25
r Gly | , 116 | בות י | Tur | 343 | | ሞም | Gln | Dhe | 343 | _ | G L | Leu | LON | 3440 | |
| | 2 01) | - 110 | . Alu | 344 | | Deu | | 0111 | 345 | | . JCI | Gry | шец | 345 | - | |
| Al. | a Leı | Gly | | | Asp | Pro | Asp | | | Ser | Val | Gln | _ | | Ser | |
| | | | 346 | 0 | | | | 346 | 5 | | | | 347 | 0 | | |
| | < | 210> | 5 | | | | | | | | | | | | | |
| | < | 211> | 819 | 1 | | | | | | | | | | | | |
| | | | DNA | | | | | | | | | | | | | |
| | < | 213> | Cen | arcn | aeum | sym | bios | um | | | | | | | | |
| | < | 220> | | | | | | | | | | | | | | |
| | | | CDS | | | | | | | | | | | | | |
| | < | 222> | (1) | (| 810) | | | | | | | | | | | |
| | < | 400> | 5 | | | | | | | | | | | | | |
| | cat | | | | | | | | | | | | | | | 48 |
| Met
1 | : His | GIY | lle | GIu
5 | GIY | GLY | Arg | Gly | Asp
10 | Met | Ser | Glu | Asn | Phe
15 | Val_ | |
| • | | | | , | | | | | 10 | | | | | 13 | | • |
| | ttt | | | | | | | | | | | | _ | _ | _ | 96 |
| Ala | a Phe | Cys | Va1
20 | | Cys | Ala | Arg | Gly
25 | Val | Thr | Lys | Asp | | Met | Lys | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| | gta | | | | | | | | | | | | | | | 144 |
| Туз | · Val | Asp
35 | Gly | Arg | Val | Phe | | Lys | Glu | Cys | His | | Arg | His | Gly | |
| | | 23 | | | | | 40 | | | | | 45 | | | | |
| | cag | | | | | | | | | | | | | | | 192 |
| Gly | Gln
50 | | Arg | Phe | Pro | | Pro | Glu | Val | Glu | | Arg | Val | Ala | Glu | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| | aag | | | | | | | | | | | | | | | 240 |
| | Lys | Val | Asp | Leu | | Gln | Met | Arg | Asn | | Leu | Ala | Glu | Met | | |
| 65 | • | | | | 70 | | | | | 75 | | | | | 80 | |
| | gcg | | | | | | | | | | | | | | | 288 |
| Arg | Ala | Ser | Gly | | Gly | Gly | Val | His | | Ser | Ala | Thr | Ser | | Ala | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| gag | gcc | gag | cag | cac | agg | gcc | gag | cta | aag | gta | cag | ctg | gtg | cag | atg | 336 |
| | Ala | | | | | | | | | | | | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| aga | aac | caq | cta | qcc | gag | ato | aac | agg | aaσ | acc | caa | gga | aaσ | cca | aca | 384 |
| | Asn | | | | | | | | | | | | | | | 204 |
| | | 115 | | | | | 120 | - | - | | | 125 | - | | | |
| caa | 222 | 224 | acc | ac. | acc | 220 | 20+ | ~~ | | 200 | 22~ | 200 | ~~~ | 225 | | 430 |
| | aaa
Lys | | | | | | | | | | | | | | | 432 |
| - | 130 | _ | | | • | 135 | | | - | _ | 140 | | • | | - 4 - | |
| | | | | | | | | | | | | | | | | |

| | Va] | | | | | Gly | | | | | Gly | | - | | 999
Gly
160 | 480 |
|-----------|-----------|------------------------------|------------|-----------|-----------|------|------------|------------|-----------|-----------|-----------|-----------|------------|-----------|-------------------|-----|
| | | agg
Arg | | | | | | | | Ala | | | | | Thr | 528 |
| | | aag
Lys | | | | | | | | | | | | Ala | | 576 |
| | | agg
Arg
195 | _ | | | | | | | | | | _ | | _ | 624 |
| | | agg
Arg | | | | | | | | | | | | | | 672 |
| _ | | acg
Thr | | | | _ | | | _ | _ | - | _ | _ | _ | | 720 |
| | | aca
Thr | | | | | | | | | | | | | | 768 |
| | | agg
Arg | | | | | | | | | | | tag
* | | | 810 |
| cct | gctg | at | | | | | | | | | | | | | | 819 |
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<: | 210>
211>
212>
213> | 269
PRT | rcha | eum | symb | oiosi | ım | | | | | | | | |
| | | 100> | | | | | | | | | | | | | | |
| Met
1 | His | Gly | Ile | Glu
5 | Gly | Gly | Arg | Gly | Asp
10 | Met | Ser | Glu | Asn | Phe
15 | Val | |
| Ala | Phe | Cys | Val
20 | Ala | Сув | Ala | Arg | Gly
25 | Val | Thr | Lys | Asp | Glu
30 | | Lys | |
| Tyr | Val | Asp
35 | Gly | Arg | Val | | His
40 | Lys | Glu | Cys | His | Ala
45 | Arg | His | Gly | |
| Gly | Gln
50 | Ile | Arg | Phe | Pro | | | Glu | Val | | Gln
60 | | Val | Ala | Glu | |
| Leu
65 | Lys | Val | Asp | Leu | Ile
70 | Gln | Met | Arg | Asn | Gln
75 | Leu | Ala | Glu | | Asn
80 | |
| Arg | Ala | Ser | - | Asp
85 | Gly | Gly | Val | His | Ser
90 | Ser | Ala | Thr | Ser | | | |
| Glu | Ala | Glu | | | Arg | Ala | Glu | Leu
105 | | Val | Gln | | Val
110 | | Met | |
| Arg | Asn | Gln
115 | | Ala | Glu | | Asn
120 | | Lys | Ala | Pro | | | Pro | Ala | |
| Arg | Lys | Lys | Ala . | Ala | Gly | | | Ala | Arg | Arg | Lys | | Gly | Lys | Lys | |

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| mh ~ | 130 | | 3 | . • | . m\ | 135 | | | mb | | 140 | | | | | |
|-------------------|-------------------|-------------------|---------------------------------|-------------------------|--------------------------|--------------------------|-------------------|--------------------------|------------------|------------|-------------------|------------|-------------------|------------------|-------------------|------------|
| 145 | | Arg | Arg | LLYS | 150 | _ | гув | Arg | Thr | 155 | _ | гуs | гуу | ALE | Gly | |
| | | 7.~~ | 1 | mb- | | | T | 7 | mh~ | | | N | | | 160 | |
| | | | | 165 | ; | | - | | 170 | | | | | 175 | | |
| Ala | Lys | Lys | Ala
180 | | Gly | Arg | Lys | Ala
185 | _ | Ala | Arg | Arg | Lys
190 | | Thr | |
| Val | Lys | Arg
195 | Thr | Val | His | Lys | Lys
200 | | Gly | Val | Arg | Arg
205 | | Thr | Thr | |
| Ala | Arg
210 | Arg | Thr | Ala | Gly | Lys
215 | Ser | Thr | Val | Arg | Arg
220 | Lys | Ser | Thr | Val | |
| Lys
225 | | Thr | Val | His | Arg
230 | _ | Thr | Gly | Lys | Lys
235 | Ala | Val | Val | Arg | Arg
240 | |
| | | Thr | Val | Lys
245 | Arg | | Ala | Arg | Arg
250 | | Ala | Gly | Arg | Lys
255 | Thr | |
| Pro | Gly | Arg | | | | Arg | Ala | _ | | Lys | Arg | Arg | | 233 | | |
| | | | 260 | | | | | 265 | | | | | | | | |
| | | 210> | | ۵ | | | | | | | | | | | | |
| | | 211> | | 3 | | | | | | | | | | | | |
| | | 212> | | arch | 3611M | syml | hios | 1177 | | | | | | | | |
| | • | | CCII | 41 (11 | acu | S y iii | 0100 | u | | | | | | | | |
| | | 220> | | | | | | | | | | | | | | |
| | | 221> | | | | | | | | | | | | | | |
| | < 7 | 222> | (1) | (| 1569 |) | | | | | | | | | | |
| | < | 100> | 7 | | | | | | | | | | | | | |
| | | | | | | | | | | | | | ata | | | 48 |
| | Gln | Ser | Leu | _ | Arg | Leu | Asp | Glu | | Cys | Ala | Glu | Ile | | Arg | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| agc | ctg | ctt | gaa | tac | gag | tcc | ccc | acc | gcc | ggt | gat | qtc | cgg | acq | gag | 96 |
| | | | | | - | | | | _ | | _ | _ | Arg | _ | | |
| | | | 20 | - | | | | 25 | | - | - | | 30 | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | _ | | | cca | _ | | 144 |
| TIE | Arg | 35 | AIA | Cys | Int | гуя | 40 | ser | Ten | Arg | Arg | 45 | Pro | гÀè | Asn | |
| | | 3,5 | | | | | 10 | | | | | 43 | | | | |
| | | | | | | | | | | | | | agg | | | 192 |
| Arg | | Ile | Leu | Ala | Thr | | Arg | Gly | Gln | Asp | Phe | Asp | Arg | Leu | Arg | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| ccc | cta | cta | ctc | aaa | аад | CCC | σta | ааσ | acc | gca | tee | aaa | gtg | acc | ata | 240 |
| | | | | | | | | | | | | | Val | | | 240 |
| 65 | | | | - | 70 | | | • | | 75 | | - | . – | | 80 | |
| | | | | | | | | | | | | | | | | |
| | | | | | atq | ccg | | | | | | | | | | 288 |
| | gca | | | | | | | | | | Ulle | GIV | Ara | Cve | mb~~ | |
| | | | | Pro | | Pro | Tyr | Ala | | PIU | 1115 | - 7 | •••• | - | IIII | |
| | | | | | | | Tyr | Ala | 90 | PIO | 1112 | 51 | | 95 | IIII | |
| Ile | Ala | Val | Met | Pro
85 | Met | Pro | | | 90 | • | | | | 95 | | 226 |
| Ile | Ala | Val
ccc | Met
ggc | Pro
85
999 | Met
gag | Pro
gcg | tcg | aac | 90
aca | ccc | aac | agc | tat
Tyr | 95
acc | ggc | 336 |
| Ile | Ala | Val
ccc | Met
ggc | Pro
85
999 | Met
gag | Pro
gcg | tcg | aac | 90
aca | ccc | aac | agc | tat | 95
acc | ggc | 336 |
| Ile
tac
Tyr | Ala
tgc
Cys | val
ccc
Pro | ggc
Gly
100 | gly
ggg
85
Pro | Met
gag
Glu | Pro
gcg
Ala | tcg
Ser | aac
Asn
105 | 90
aca
Thr | ccc
Pro | aac
Asn | agc
Ser | tat
Tyr
110 | 95
acc
Thr | ggc
Gly | 336 |
| Ile
tac
Tyr | Ala
tgc
Cys | val
ccc
Pro | Met
ggc
Gly
100
ata | Pro
85
ggg
Gly | Met
gag
Glu
gcg | Pro
gcg
Ala
ggc | tog
Ser
goo | aac
Asn
105
atg | 90
aca
Thr | ccc
Pro | aac
Asn
ggg | agc
Ser | tat
Tyr | 95
acc
Thr | ggc
Gly
gaa | 336
384 |

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| | | 115 | | | | 120 | | | | | 125 | | | | |
|---|---|-----|---|---|-------|-----|---|---|---|-------------------|-----|---|-----|-------------------|------|
| | | Val | | | | Ala | | | | | His | | | gat
Asp | 432 |
| | | | | _ | Val | | | | | Thr | | _ | | atg
Met
160 | 480 |
| _ | _ | _ | | _ |
 | | _ | _ | | _ | | - | _ | ctc
Leu | 528 |
| | | | _ | |
 | _ | | | - | _ | | _ | | gaa
Glu | 576 |
| | - | | | - | - | | | | | gag
Glu | | _ | | _ | 624 |
| | _ | | | | | - | | _ | | ggc
Gly
220 | | | _ | _ | 672 |
| _ | | | | |
_ | _ | | | | gag
Glu | - | | _ | | 720 |
| - | | | | | | - | - | | | gag
Glu | _ | | _ | _ | 768 |
| | | | | | | | | | | atg
Met | | | | | 816 |
| | | | | | | | | | | ctg
Leu | | | | | 864 |
| | | | | | | | | | | gtg
Val
300 | | | | | 912 |
| | | | | | | | | | | tcg
Ser | | | Glu | | 960 |
| | | | | | | | | | | ctc
Leu | | | | | 1008 |
| | | | | | | | | | | gtg
Val | | | | | 1056 |

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| | | | | | | | | | | | | | Leu | | cag
Gln | 1104 |
|----------|-------------------|--------------------------|------------|----------|----------|------|-------|------------|-----------|-----|-----------|-----|-----------|-----------|-------------------|------|
| _ | | | _ | | | | | | | | _ | Cys | _ | _ | ata
Ile | 1152 |
| | _ | | | | | | | | | | _ | _ | _ | _ | ctc
Leu
400 | 1200 |
| _ | att
Ile | _ | | | - | | _ | _ | _ | | | _ | _ | _ | | 1248 |
| | tcg
Ser | | _ | _ | | _ | _ | _ | | | | | | _ | ctg
Leu | 1296 |
| _ | aag
Lys | | | | - | _ | | | _ | | _ | | _ | _ | | 1344 |
| | ata
Ile
450 | | | | | | | | | | | | | | | 1392 |
| | agg
Arg | | | | _ | | _ | | | | _ | | | _ | | 1440 |
| | gca
Ala | | | | | | | | | | | | | | _ | 1488 |
| | agc
Ser | _ | - | | | | | | | _ | | | | | | 1536 |
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Thr | | | | - | | _ | | | _ | | | | | | 1569 |
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11>
12>
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PRT | rcha | eum | symb | oiosu | .m | | | | | | | | |
| | _ | 00> | - | a) | 3 | • - | | ~ 1 | | ο. | - 1 | ~3 | > | _ | | |
| Met
1 | Gln | ser | ьеи | 2
GTÀ | Arg | ren. | Asp | GLU | Ala
10 | Cys | Ala | Glu | Ile | Ser
15 | Arg | |
| Ser | Leu | | Glu
20 | Tyr | Glu | Ser | | Thr
25 | | Gly | Asp | | _ | | Glu | |
| Ile | Arg | | | Cys | Thr | - | | | Leu | Arg | Arg | | 30
Pro | Lys | Asn | |
| Arg | Glu
50 | | Leu | Ala | Thr | | | Gly | Gln | Asp | Phe
60 | | Arg | Leu | Arg | |

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Pro Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 90 Tyr Cys Pro Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 105 Gly Glu Pro Ile Ala Ala Gly Ala Met Asn Ser Gly Tyr Asp Pro Glu 120 Glu Gln Val Arg Ala Gly Leu Ala Arg Leu Arg Ala His Gly His Asp 135 Val Ala Lys Leu Glu Ile Val Ile Val Gly Gly Thr Phe Leu Phe Met 150 Pro Gln Glu Tyr Gln Glu Trp Phe Val Lys Ser Cys Tyr Asp Ala Leu 165 170 Asn Gly Ser Ala Ser Ala Gly Met Glu Glu Ala Lys His Arg Asn Glu 185 Thr Ala Val His Arg Asn Val Gly Leu Thr Ile Glu Thr Lys Pro Asp 200 Tyr Cys Arg Thr Glu His Val Asp Ala Met Leu Gly Phe Gly Ala Thr 215 220 Arg Val Glu Ile Gly Val Gln Ser Leu Arg Glu Glu Val Tyr Leu Arg 230 235 Val Asn Arg Gly His Gly Tyr Gln Asp Val Thr Glu Ser Phe Ala Ala 245 250 Ala Arg Asp Ala Gly Tyr Lys Val Ala Ala His Met Met Pro Gly Leu 265 260 Pro Gly Ala Thr Pro Glu Gly Asp Ile Glu Asp Leu Arg Met Leu Phe 280 Glu Asp Pro Ala Leu Arg Pro Asp Met Leu Lys Val Tyr Pro Ala Leu 295 300 Val Val Arg Gly Thr Pro Met Tyr Glu Glu Tyr Ser Arg Gly Glu Tyr Ser Pro Tyr Thr Glu Glu Glu Val Ile Arg Val Leu Ser Glu Ala Lys 325 330 Ala Arg Val Pro Arg Trp Ala Arg Ile Met Arg Val Gln Arg Glu Ile 345 His Pro Asp Glu Ile Val Ala Gly Pro Arg Ser Gly Asn Leu Arg Gln 360 Leu Val His Lys Arg Leu Gln Glu Gln Gly Arg Arg Cys Arg Cys Ile 375 Arg Cys Arg Glu Ala Gly Leu Ala Gly Arg Thr Val Pro Gln Lys Leu 390 395 Arg Ile Asp Arg Ala Asp Tyr Ser Ala Ser Gly Gly Arg Glu Ser Phe Ile Ser Leu Val Asp Gly Asp Asp Ala Ile Tyr Gly Phe Val Arg Leu 425 Arg Lys Pro Ser Gly Ala Ala His Arg Pro Glu Val Thr Pro Glu Ser 440 Cys Ile Ile Arg Glu Leu His Val Tyr Gly Arg Ser Leu Gly Leu Gly 455 Glu Arg Gly Gly Ile Gln His Ser Gly Leu Gly Arg Arg Leu Val Ser 470 475 Glu Ala Glu Ser Ala Ala Arg Glu Leu Gly Ala Gly Arg Leu Leu Val 490 Ile Ser Ala Val Gly Thr Arg Gly Tyr Tyr Arg Arg Leu Gly Tyr Ser 500 505 Arg Thr Gly Pro Tyr Met Gly Lys Val Leu

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221> | DNA
Cena | arch | 1675) | | bios | 1 m | | | | | | | | |
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| | gag | | ata | | cgc
Arg | | | | | | | | | | | 48 |
| | | | | | gag
Glu | | | | | | | | | | | 96 |
| | | | | | ggc | | | | | | | | | | | 144 |
| Gly
999 | gat
Asp
50 | gca
Ala | gtc
Val | agg
Arg | gcg
Ala | tac
Tyr
55 | ggc | gtg
Val | gjy
ggg | ctc
Leu | gcc
Ala
60 | gtc
Val | ggc
Gly | gac
Asp | atg
Met | 192 |
| | | | | | ctc
Leu
70 | | | | | | | | | | | 240 |
| cgc
Arg | aag
Lys | gtc
Val | ccc
Pro | gag
Glu
85 | ggc
gly | atg
Met | cca
Pro | tcc
Ser | tcg
Ser
90 | cta
Leu | gaa
Glu | gag
Glu | cac
His | ata
Ile
95 | gcc
Ala | 288 |
| | | | | | ata
Ile | | | | | | | | | | | 336 |
| | | | | | ggc | | | | | | | | | | | 384 |
| | | | | | agg
Arg | | | | | | | | | | | 432 |
| | | | | | cac
His
150 | | | | | | | | | | | 480 |
| gag
Glu | aag
Lys | ata
Ile | gcc
Ala | gag
Glu
165 | atg
Met | gtg
Val | ggc
Gly | cag
Gln | gaa
Glu
170 | aag
Lys | ttt
Phe | cgc
Arg | agc
Ser | agc
Ser
175 | ctg
Leu | 528 |
| _ | | | _ | _ | tgt
Cys | _ | | _ | | | | | | | | 576 |

WO 00/18909

| | | | | | | gac
Asp | | | | | | | | | ggc
Gly | 624 |
|------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------|
| | | | | | | aga
Arg
215 | | | | | | | | | ggc
Gly | 672 |
| | | | | | | gcc
Ala | | | | | | | | | | 720 |
| | | | | | | gcg
Ala | | | | | | | | | | 768 |
| | | | | | | gta
Val | | | | | | | | | | 816 |
| Ile | Leu | Ser
275 | Ser | Pro | His | ccc
Pro | His
280 | His | Thr | Arg | Tyr | Glu
285 | Met | Phe | Leu | 864 |
| Asp | Lys
290 | Gly | Gly | Lys | Lys | ata
Ile
295 | Ser | Lys | Ser | Ser | Gly
300 | Asn | Val | Val | Thr | 912 |
| Pro
305 | Gln | Lys | Trp | Leu | Arg
310 | tac
Tyr | Gly | Thr | Pro | Gln
315 | Ser | Ile | Leu | Leu | Leu
320 | 960 |
| Met | Tyr | Lys | Arg | Ile
325 | Thr | Gly
999 | Ala | Arg | Glu
330 | Leu | Gly | Leu | Glu | Asp
335 | Val | 1008 |
| Pro | Ser | Leu | Met
340 | Asp | Glu | tac
Tyr | Gly | Asp
345 | Leu | Gln | Arg | Glu | Tyr
350 | Phe | Ala | 1056 |
| Gly | Gly | Gly
355 | Arg | Gly | Gly | aaa
Lys | Ala
360 | Arg | Glu | Ala | Lys | Asn
365 | Arg | Gly | Leu | 1104 |
| Phe | Glu
370 | Tyr | Thr | Asn | Leu | ctg
Leu
375 | Glu | Ala | Gln | Glu | Gly
380 | Pro | Arg | Pro | His | 1152 |
| Ala
385 | Gly | Tyr | Arg | Leu | Leu
390 | gtc
Val | Glu | Leu | Ser | Arg
395 | Leu | Phe | Arg | Glu | Asn
400 | 1200 |
| | | | | | | aaa
Lys | | | | | | | | | | 1248 |
| ggg | CCC | tcg | CCC | ggg | atc | gag | cgg | ctc | ata | gca | ctg | gcc | gga | aac | tat | 1296 |

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Gly Pro Ser Pro Gly Ile Glu Arg Leu Ile Ala Leu Ala Gly Asn Tyr gca gac gac atg tat tot gcc gag aga aca gag gtg gag ott gac ggg 1344 Ala Asp Asp Met Tyr Ser Ala Glu Arg Thr Glu Val Glu Leu Asp Gly 440 gec aca agg ggg gec etc teg gag etg gea gaa atg etc ggt tee gee 1392 Ala Thr Arg Gly Ala Leu Ser Glu Leu Ala Glu Met Leu Gly Ser Ala 450 455 460 ccg gag ggc gga ctg cag gat gtc ata tac ggc gtg gcc aag tcc cac 1440 Pro Glu Gly Gly Leu Gln Asp Val Ile Tyr Gly Val Ala Lys Ser His 465 470 475 ggg gtg ccc ccg cgc gac ttt ttc aag gcg ctg tac agg ata ata ctg 1488 Gly Val Pro Pro Arg Asp Phe Phe Lys Ala Leu Tyr Arg Ile Ile Leu 485 gat gca tcc agc ggg ccg agg ata ggc ccc ttc ata gag gac ata ggc 1536 Asp Ala Ser Ser Gly Pro Arg Ile Gly Pro Phe Ile Glu Asp Ile Gly 500 agg gag aag gtg gca ggt atg ata cgg ggg cgc ctc tga 1575 Arg Glu Lys Val Ala Gly Met Ile Arg Gly Arg Leu * 515 <210> 10 <211> 524 <212> PRT <213> Cenarchaeum symbiosum <400> 10 Met Glu Thr Ile Gly Arg Gly Thr Trp Ile Asp Lys Leu Ala His Glu 1 5 Leu Val Glu Arg Glu Glu Ala Leu Gly Arg Asp Thr Glu Met Ile Asn 25 Val Glu Ser Gly Leu Gly Ala Ser Gly Ile Pro His Met Gly Ser Leu Gly Asp Ala Val Arg Ala Tyr Gly Val Gly Leu Ala Val Gly Asp Met Gly His Ser Phe Arg Leu Ile Ala Tyr Phe Asp Asp Leu Asp Gly Leu 70 Arg Lys Val Pro Glu Gly Met Pro Ser Ser Leu Glu Glu His Ile Ala 85 90 Arg Pro Val Ser Ala Ile Pro Asp Pro Tyr Gly Cys His Asp Ser Tyr 105 Gly Met His Met Ser Gly Leu Leu Leu Glu Gly Leu Asp Ala Leu Gly 120 Ile Glu Tyr Asp Phe Arg Arg Ala Arg Asp Thr Tyr Arg Asp Gly Leu 135 140 Leu Ala Glu Gln Ile His Arg Ile Leu Ser Asn Ser Ser Val Ile Gly Glu Lys Ile Ala Glu Met Val Gly Gln Glu Lys Phe Arg Ser Ser Leu 165 170 Pro Tyr Phe Ala Val Cys Glu Gln Cys Gly Lys Met Tyr Thr Ala Glu 185

Ser Val Glu Tyr Leu Ala Asp Ser Arg Lys Val Arg Tyr Arg Cys Gly

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200
 Asp Ala Glu Val Gly Gly Arg Lys Ile Ala Gly Cys Gly His Glu Gly
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 Glu Ala Asp Thr Gly Gly Ala Gly Gly Lys Leu Ala Trp Lys Val Glu
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                                        235
Phe Ala Ala Arg Trp Gln Ala Phe Asp Val Arg Phe Glu Ala Tyr Gly
                                    250
Lys Asp Ile Met Asp Ser Val Arg Ile Asn Asp Trp Val Ser Asp Glu
                                265
Ile Leu Ser Ser Pro His Pro His His Thr Arg Tyr Glu Met Phe Leu
                            280
                                                285
Asp Lys Gly Gly Lys Lys Ile Ser Lys Ser Ser Gly Asn Val Val Thr
                        295
                                            300
Pro Gln Lys Trp Leu Arg Tyr Gly Thr Pro Gln Ser Ile Leu Leu Leu
                    310
                                        315
Met Tyr Lys Arg Ile Thr Gly Ala Arg Glu Leu Gly Leu Glu Asp Val
                                    330
Pro Ser Leu Met Asp Glu Tyr Gly Asp Leu Gln Arg Glu Tyr Phe Ala
                                345
Gly Gly Arg Gly Gly Lys Ala Arg Glu Ala Lys Asn Arg Gly Leu
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Phe Glu Tyr Thr Asn Leu Leu Glu Ala Gln Glu Gly Pro Arg Pro His
                        375
                                            380
Ala Gly Tyr Arg Leu Leu Val Glu Leu Ser Arg Leu Phe Arg Glu Asn
                390
                                        395
Arg Thr Glu Arg Val Thr Lys Lys Leu Val Glu Tyr Gly Val Ile Asp
                405
                                    410
Gly Pro Ser Pro Gly Ile Glu Arg Leu Ile Ala Leu Ala Gly Asn Tyr
            420
                                425
Ala Asp Asp Met Tyr Ser Ala Glu Arg Thr Glu Val Glu Leu Asp Gly
Ala Thr Arg Gly Ala Leu Ser Glu Leu Ala Glu Met Leu Gly Ser Ala
                        455
Pro Glu Gly Gly Leu Gln Asp Val Ile Tyr Gly Val Ala Lys Ser His
                                        475
Gly Val Pro Pro Arg Asp Phe Phe Lys Ala Leu Tyr Arg Ile Ile Leu
                485
                                   490
Asp Ala Ser Ser Gly Pro Arg Ile Gly Pro Phe Ile Glu Asp Ile Gly
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Met Glu Ser Ala Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr
1
ctt tca aaa ttg caa cag tat tcg ggg agg gac aca att cta tat gcg
```

Leu Ser Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala

| | | 20 | 1 | | | | 25 | i | | | | 30 |) | | | |
|-----|-----|-----|---|-----|---|---|-----|-----|---|---|-------------------|-----|---|------------------|-------|----|
| | | Met | _ | _ | _ | _ | His | _ | | | _ | Ala | | ata
Ile | 1 | 44 |
| | Gly | | | | | | | | | | Arg | | | aag
Lys | 19 | 92 |
| Lys | | | | | | | | | | | ggt | | - | gag
Glu
80 | 24 | 40 |
| - | _ | _ | | _ | | | | | | | tat
Tyr | _ | _ | | 28 | 98 |
| | | | | | | | | | | | tcg
Ser | | | | 33 | 36 |
| | | | | | | | | | | _ | tct
Ser
125 | | | | 38 | 14 |
| | | | | | | | | | | | atg
Met | | | | 43 | 2 |
| | | | | | | | | | | | cag
Gln | | | | 48 | 0 |
| | | _ | | | | | _ | | | | ttg
Leu | | | | 52 | 8 |
| | | | _ | _ | | | | | _ | - | cag
Gln | | | _ | 57 | 6 |
| | | | | | | | | | | | ttt
Phe
205 | | | | . 624 | 4 |
| | | | | Lys | | | | | | | atg
Met | | | | 672 | 2 |
| | | | | | | | | Tyr | | | cga
Arg | | | | 720 | 0 |
| | | Gly | | | | | Asp | | | | gac
Asp | Gln | | | 768 | 3 |

PCT/US99/22752

WO 00/18909 -58cag gat ctg aca ttg tcg gta tct cat gca gcg gat atc ctg tct caa 816 Gln Asp Leu Thr Leu Ser Val Ser His Ala Ala Asp Ile Leu Ser Gln 260 ttt act cca atc aac aaa atc atc gcg aat cac ctc ggt aat tca gtt 864 Phe Thr Pro Ile Asn Lys Ile Ile Ala Asn His Leu Gly Asn Ser Val atc agc aaa cca tca aca tag 885 Ile Ser Lys Pro Ser Thr * 290 <210> 12 <211> 294 <212> PRT <213> Cenarchaeum sybiosum <400> 12 Met Glu Ser Ala Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr 10 Leu Ser Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala 25 Thr Asn Trp Met Thr Asp Glu Pro His Thr Pro Asn Glu Ala Leu Ile 40 Thr Asn Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys 55 60 Thr Lys Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Ala Glu 70 Ser Ala Glu Ser Ile Val Thr Tyr Leu His Ala Lys Tyr Asp Asp Ile 90 Arg Val Ile Ile Pro Tyr Ala Ala Met Ser Ala Ala Ser Met Leu Ala 105 Cys Ala Ser Asn Ser Leu Val Met Gly Lys His Ser Ser Ile Gly Pro 120 Ala Asp Pro Gln Phe Ile Phe Pro Thr Lys Ile Gly Met Gln Ile Met 135 Ser Ala Gln Leu Leu Ile Asp Glu Leu Gln Glu Val Gln Val Val Ser 150 155 Glu Lys His Pro Gly Arg Leu Gly Ala Trp Leu Pro Leu Leu Gly Gln 170 Tyr Pro Pro Gly Leu Val Gln Lys Cys Ile Ser Ser Gln Lys Leu Ala 180 185 Glu Val Leu Val Gln Lys Trp Leu Glu Asp His Met Phe Ala Gly Glu 200 Ser Asp Ala Ala Glu Lys Ser Lys Lys Ile Ser Gly Met Leu Ala Ser

215 Pro Gly Lys Tyr Tyr Ser His Gly Arg Tyr Ile Ser Arg Glu Glu Cys

235

Arg Gly Ile Gly Leu Lys Ile Thr Asp Leu Glu Ala Asp Gln Glu Phe 250 Gln Asp Leu Thr Leu Ser Val Ser His Ala Ala Asp Ile Leu Ser Gln

265 Phe Thr Pro Ile Asn Lys Ile Ile Ala Asn His Leu Gly Asn Ser Val

280

Ile Ser Lys Pro Ser Thr

-59-

<211> 1305 <212> DNA <213> Cenarchaem symbiosum <220> <221> CDS <222> (1) ... (1305) <400> 13 gtg gat cta gag cgc gag tac agg gca aag acc agg ggc tcg gcg ggg 48 Met Asp Leu Glu Arg Glu Tyr Arg Ala Lys Thr Arg Gly Ser Ala Gly ata ttt gcc cgg tcg aga agg tac cat gta ggg ggg gtc agc cac aac Ile Phe Ala Arg Ser Arg Arg Tyr His Val Gly Gly Val Ser His Asn 20 ata agg tac tat gag ccq tac ccq ttt gtt aca agg tcq qcq cqc qqc 144 Ile Arg Tyr Tyr Glu Pro Tyr Pro Phe Val Thr Arg Ser Ala Arg Gly 35 40 aag cac ctt gtg gac gtc gac ggg aac aag tat acc gac tat tgg atg 192 Lys His Leu Val Asp Val Asp Gly Asn Lys Tyr Thr Asp Tyr Trp Met ggg cac tgg agc ctg ata ctc ggc cac gcg ccg gcg caa gta agg tcq 240 Gly His Trp Ser Leu Ile Leu Gly His Ala Pro Ala Gln Val Arg Ser gca gtg gag ggg cag ctg cgc cgc ggc tgg ata cac ggg acc gca aac 288 Ala Val Glu Gly Gln Leu Arg Arg Gly Trp Ile His Gly Thr Ala Asn 90 gag ccc acc atg cgg ctc tcg gag atc ata cgc ggg gcg gta aag gcg 336 Glu Pro Thr Met Arg Leu Ser Glu Ile Ile Arg Gly Ala Val Lys Ala 100 105 gca gag aag ata agg tat gtt aca tcc ggc acg gag gcc gtc atg tat 384 Ala Glu Lys Ile Arg Tyr Val Thr Ser Gly Thr Glu Ala Val Met Tyr 115 gcg gca agg atg gcg cgc gca cgc acg gga aaa aaa gtg ata gca aag 432 Ala Ala Arg Met Ala Arg Ala Arg Thr Gly Lys Lys Val Ile Ala Lys 130 gte gae gge tgg cae gga tae geg teg ggg etg eta aag teg gte 480 Val Asp Gly Gly Trp His Gly Tyr Ala Ser Gly Leu Leu Lys Ser Val 145 150 aac tgg ccg tac gat gtg ccc gag agc ggg ggg ctc gtc gac gag gag 528 Asn Trp Pro Tyr Asp Val Pro Glu Ser Gly Gly Leu Val Asp Glu Glu 165 170 cac acc gtg tcc atc ccg tac aac aat ctg gag gga tcc ctg gag gcg 576 His Thr Val Ser Ile Pro Tyr Asn Asn Leu Glu Gly Ser Leu Glu Ala 180 185 cta agg cgc gca ggg ggc gac ctt gca tgt gtc ata gtc gag ccg atg 624

--60-

| Leu | Arg | 195 | | Gly | / Gly | / Asp | 200 | | Cys | val | l Ile | e Val
205 | | ı Pro |) Met | |
|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|-------------------|------------|------------|-------------------|------|
| | | Gly | | | | | Pro | | | | | туг | | | ggc
Gly | 672 |
| | Gln | | | | | Ser | | | | | Phe | | | | gag
Glu
240 | 720 |
| | | | | | Arg | | | | | Cys | | | | | atg
Met | 768 |
| | | | | | | | | | | | | | | Gly | gga
Gly | 816 |
| | | | | | | | | | | | | atg
Met
285 | _ | | | 864 |
| | | | | | | | | | | | | att
Ile | | | | 912 |
| | | | | | | | | | | | | gcc
Ala | | | | 960 |
| | | | | | | | | | | | | aga
Arg | | | | 1008 |
| | | | | | | | | | | | | ttc
Phe | | | | 1056 |
| | | | | | | | | | | | | cac
His
365 | | | | 1104 |
| | | | | | | | | | | | | gcc
Ala | | | | 1152 |
| gtg
Val
385 | cat
His | ctg
Leu | ctg
Leu | cac
His | agg
Arg
390 | tac
Tyr | cac
His | ctg
Leu | gac
Asp | atg
Met
395 | att
Ile | aca
Thr | agg
Arg | gac
Asp | ggc
Gly
400 | 1200 |
| | | | Leu | | | | | Gly | | | | gcc
Ala | | | | 1248 |
| | | Asp | | | | | Tyr | | | | | cgc
Arg | | | | 1296 |

1305

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gga ctg tga Gly Leu *

<210> 14

<211> 434

<212> PRT

<213> Cenarchaem symbiosum

<400> 14

Met Asp Leu Glu Arg Glu Tyr Arg Ala Lys Thr Arg Gly Ser Ala Gly Ile Phe Ala Arg Ser Arg Arg Tyr His Val Gly Gly Val Ser His Asn 25 Ile Arg Tyr Tyr Glu Pro Tyr Pro Phe Val Thr Arg Ser Ala Arg Gly Lys His Leu Val Asp Val Asp Gly Asn Lys Tyr Thr Asp Tyr Trp Met Gly His Trp Ser Leu Ile Leu Gly His Ala Pro Ala Gln Val Arg Ser Ala Val Glu Gly Gln Leu Arg Arg Gly Trp Ile His Gly Thr Ala Asn 90 Glu Pro Thr Met Arg Leu Ser Glu Ile Ile Arg Gly Ala Val Lys Ala Ala Glu Lys Ile Arg Tyr Val Thr Ser Gly Thr Glu Ala Val Met Tyr 120 Ala Ala Arg Met Ala Arg Ala Arg Thr Gly Lys Lys Val Ile Ala Lys 135 Val Asp Gly Gly Trp His Gly Tyr Ala Ser Gly Leu Leu Lys Ser Val 150 155 Asn Trp Pro Tyr Asp Val Pro Glu Ser Gly Gly Leu Val Asp Glu Glu 165 170 His Thr Val Ser Ile Pro Tyr Asn Asn Leu Glu Gly Ser Leu Glu Ala 185 Leu Arg Arg Ala Gly Gly Asp Leu Ala Cys Val Ile Val Glu Pro Met 200 Leu Gly Gly Gly Cys Ile Pro Ala Glu Pro Asp Tyr Leu Arg Gly 215 220 Ile Gln Glu Phe Val His Ser Lys Gly Ala Leu Phe Ile Leu Asp Glu 230 235 Ile Val Thr Gly Phe Arg Phe Asp Phe Gly Cys Ala Tyr Lys Lys Met 250 Gly Leu Asp Pro Asp Val Val Ala Leu Gly Lys Ile Val Gly Gly 265 Phe Pro Ile Gly Val Val Cys Gly Lys Asp Glu Val Met Cys Ile Ser 280 Asp Thr Gly Ala His Ala Arg Thr Glu Arg Ala Tyr Ile Gly Gly Gly 295 Thr Phe Ser Ala Asn Pro Ala Thr Met Thr Ala Gly Ala Ala Ala Leu 310 315 Gly Ala Leu Arg Glu Arg Arg Gly Thr Leu Tyr Pro Arg Ile Asn Ser 330 Met Gly Asp Asp Ala Arg Ala Arg Leu Ser Arg Ile Phe Asp Gly Arg 345 Val Ala Val Thr Gly Arg Gly Ser Leu Phe Met Thr His Phe Thr Pro 360 365 Asp Gly Ala Arg Arg Ile Ser Ser Ala Ala Asp Ala Ala Cys Asp

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Val His Leu Leu His Arg Tyr His Leu Asp Met Ile Thr Arg Asp Gly 390 395 Ile Phe Phe Leu Pro Gly Lys Leu Gly Ala Ile Ser Ala Ala His Ser 405 410 Arg Ala Asp Leu Gly Ala Met Tyr Ser Ala Ser Glu Arg Phe Ala Gly 425 Gly Leu <210> 15 <211> 816 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(816) <400> 15 atg ata etc tte gge aag age gae eec tee gae etg etc ege eag gee 48 Met Ile Leu Phe Gly Lys Ser Asp Pro Ser Asp Leu Leu Arg Gln Ala gat ctt ttg tgc agt ggg aac aag tac aag gcg gca gtg ggc ctg tac 96 Asp Leu Leu Cys Ser Gly Asn Lys Tyr Lys Ala Ala Val Gly Leu Tyr 20 25 age agg ata etc aag gae gae eeg eag aac agg atg gte etg eag aga Ser Arg Ile Leu Lys Asp Asp Pro Gln Asn Arg Met Val Leu Gln Arg 35 aag ggc ctc gcc ctc aac agg ata aga agg tac tct gat gcc ata acg 192 Lys Gly Leu Ala Leu Asn Arg Ile Arg Arg Tyr Ser Asp Ala Ile Thr 50 55 tgc ttt gat ctg ctc gag ctg gat gat ggc gac gcg cct gca tac 240 Cys Phe Asp Leu Leu Leu Glu Leu Asp Asp Gly Asp Ala Pro Ala Tyr 65 75 aac aac aag gee ata gee eag gee gag etg gge gat aeg gea tee gee 288 Asn Asn Lys Ala Ile Ala Gln Ala Glu Leu Gly Asp Thr Ala Ser Ala 90 ctg gag aac tat ggc agg gcc atc gaa gcc agc ccc agg tac gcg ccg 336 Leu Glu Asn Tyr Gly Arg Ala Ile Glu Ala Ser Pro Arg Tyr Ala Pro 105 gcg tac ttt aac agg gcc gtc ctg ctc gac agg ctc ggc gag cac gaa 384 Ala Tyr Phe Asn Arg Ala Val Leu Leu Asp Arg Leu Gly Glu His Glu 115 120 gac gcg ctg ccg gac ctc gac aag gcg aca agg ctg gac agg gac aag 432 Asp Ala Leu Pro Asp Leu Asp Lys Ala Thr Arg Leu Asp Arg Asp Lys 130 135 140, gcc aac ccg agg ttc tac aag ggg ata gtc ctg gga aag atg ggc cgg 480 Ala Asn Pro Arg Phe Tyr Lys Gly Ile Val Leu Gly Lys Met Gly Arg 145

-63-

| | | | | | | | | | -63 | - | | | | | | |
|------------|-----------|------------------------------|-------------------|-----------|------------|-----------|------------|------------|-----------|------------|-----------|------------|------------|-----------|------------|-----|
| | | | | | Ser | | | | | | | | | | cac
His | 528 |
| | | | | | | | | | | | | | | | ctc
Leu | 576 |
| | | | gcc
Ala | | - | | | | | | | - | | _ | | 624 |
| | _ | | aac
Asn | | | _ | | | _ | _ | | _ | _ | | _ | 672 |
| | _ | _ | agg
Arg | | - | | | | _ | | | | _ | _ | _ | 720 |
| _ | _ | _ | tcc
Ser | _ | | | | _ | | _ | _ | _ | | _ | _ | 768 |
| | | | ata
Ile
260 | | | | | | | | | | | | taa
* | 816 |
| | <:
: | 210>
211>
212>
213> | 271 | ırcha | eum | symb | oiosu | ım | | | | | | | | |
| | <4 | 100> | 16 | | | | | | | | | | | | | |
| 1 | | | Phe | 5 | - | | _ | | 10 | | | | | 15 | | |
| Asp | Leu | Leu | Сув
20 | ser | GIÀ | ASI | гÀг | 1yr
25 | гÀг | Ala | Ата | vaı | 30
31 | Leu | Tyr | |
| Ser | Arg | Ile
35 | Leu | Lys | Asp | Asp | Pro
40 | Gln | Asn | Arg | Met | Val
45 | Leu | Gln | Arg | |
| Lys | Gly
50 | | Ala | Leu | Asn | Arg
55 | | Arg | Arg | Tyr | Ser
60 | | Ala | Ile | Thr | |
| Cys
65 | Phe | qaA | Leu | Leu | Leu
70 | Glu | Leu | Asp | qaA | Gly
75 | Asp | Ala | Pro | Ala | Tyr
80 | |
| | Asn | Lys | Ala | Ile
85 | | Gln | Ala | Glu | Leu
90 | - | Asp | Thr | Ala | Ser
95 | | |
| Leu | Glu | Asn | Tyr
100 | Gly | Arg | Ala | Ile | Glu
105 | Ala | Ser | Pro | Arg | Tyr
110 | | Pro | |
| Ala | Tyr | Phe | Asn | Arg | Ala | Val | Leu
120 | | Asp | Arg | Leu | Gly
125 | | His | Glu | |
| | 130 | | Pro | | | 135 | | | | _ | 140 | | _ | _ | - | |
| Ala
145 | Asn | Pro | Arg | Phe | Tyr
150 | Lys | Gly | Ile | | Leu
155 | Gly | Lys | Met | Gly | Arg
160 | |
| *** | 71. | C1 | 77- | T | 0 | a | Dh a | T | C1 | 17-1 | a | N | λla | 3 | *** | |

His Ala Glu Ala Leu Ser Cys Phe Lys Glu Val Cys Arg Ala Asp His

Gly His Ala Asp Ser Gln Phe His Val Ala Ile Glu Val Ala Glu Leu 185

170

190

-64-

Gly Lys His Ala Glu Ala Leu Gly Glu Leu Ala Ala Leu Pro Ala Glu 200 Tyr Arg Glu Asn Ala Asn Val Leu Tyr Ala Arg Ala Arg Ser Leu Ala 220 215 Gly Leu Asp Arg Tyr Asp Glu Ser Ile Ala His Leu Gln Lys Ala Ala 230 235 Arg Lys Asp Ser Lys Thr Ile Lys Lys Trp Ala Arg Ala Glu Lys Ala 250 Phe Asp His Ile Arg Asp Asp Pro Arg Phe Lys Lys Ile Ala Gly 260 265 <210> 17 <211> 696 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) . . . (696) <400> 17 gtg act gac aag aca agg atc atc gtc ctg cgc aac gcc atg act gaa 48 Met Thr Asp Lys Thr Arg Ile Ile Val Leu Arg Asn Ala Met Thr Glu cag tcc gcc cgg gcc atg atc gag gca aaa aag acg ggg cca ttc agg 96 Gln Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr Gly Pro Phe Arg gec atg atg agg geg eec eea aag gag gae gte eat gta eat tee qta 144 Ala Met Met Arg Ala Pro Pro Lys Glu Asp Val His Val His Ser Val agg etc gtc cac gag geg etc atc egc gtc tec gec egg tac teg qec 192 Arg Leu Val His Glu Ala Leu Ile Arg Val Ser Ala Arg Tyr Ser Ala 50 55 gac ttt ttc aga agg gcc gtg cac ccg atc aag gtg gat cag aac gtg 240 Asp Phe Phe Arg Arg Ala Val His Pro Ile Lys Val Asp Gln Asn Val 65 70 75 atc gag gtg gtg ctg ggc gac ggc gtc ttc ccg ata agg tca aag tcg 288 Ile Glu Val Val Leu Gly Asp Gly Val Phe Pro Ile Arg Ser Lys Ser 85 cgc ata cgc aag acc ctg tcc gcc ggg cgc ggc aag aac agg gtc gat 336 Arg Ile Arg Lys Thr Leu Ser Ala Gly Arg Gly Lys Asn Arg Val Asp 100 105 ctg gaa ctc gag gag cac gta tac gcg gaa tca gag ggc gtg atg tgc 384 Leu Glu Leu Glu Glu His Val Tyr Ala Glu Ser Glu Gly Val Met Cys 115 120 ctt gac cgg cac ggc ggg gag acc ggc ttt ccc tac aag acg ggg acc 432 Leu Asp Arg His Gly Gly Glu Thr Gly Phe Pro Tyr Lys Thr Gly Thr 135 ggc gcg gtc gag ccg tac ccg cgg cgc atg ctt gat tcg tcg gag aat

-65-

| Gly Ala Val Glu Pro Tyr Pro Arg Arg Met Leu Asp Ser Ser Gl
145 150 155 | u Asn
160 |
|--|---|
| gtg cgg cgc ccg gag ata gac acc ggg gtg gcg ctg gaa aaa ct
Val Arg Arg Pro Glu Ile Asp Thr Gly Val Ala Leu Glu Lys Le
165 170 17 | u Arg |
| gta aag ctc cgc ggg ccc ccg cct gac ggc atg cgc gac ctc cg
Val Lys Leu Arg Gly Pro Pro Pro Asp Gly Met Arg Asp Leu Ar
180 185 190 | |
| gag ttt gca gtc aga tcg gtc gaa gaa gtg tat gcc cct gtc ta
Glu Phe Ala Val Arg Ser Val Glu Glu Val Tyr Ala Pro Val Tyr
195 200 205 | |
| teg egg ett gtg ggg ece aaa aaa aag gte egg ata atg egg at
Ser Arg Leu Val Gly Pro Lys Lys Val Arg Ile Met Arg Ile
210 215 220 | |
| gcg gca aga aaa aag atg ctg tag
Ala Ala Arg Lys Lys Met Leu *
225 230 | 696 |
| <210> 18
<211> 231
<212> PRT
<213> Cenarchaeum symbiosum | |
| <400> 18 | |
| - Mark 1976 Nove From 1986 Nove File File Mail From Nove Nove Nie Mark 1986- | . ~1 |
| Met Thr Asp Lys Thr Arg Ile Ile Val Leu Arg Asn Ala Met Thi
1 5 10 15 | |
| | |
| 1 5 10 15 Gln Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr Gly Pro Phe 20 25 30 Ala Met Met Arg Ala Pro Pro Lys Glu Asp Val His Val His Ser | a Arg |
| 1 5 15 16 17 18 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19 | e Arg |
| 1 | e Arg Val Ala Val |
| 1 5 15 16 17 18 18 18 19 19 19 19 19 19 19 19 19 19 19 19 19 | e Arg Val Ala Val 80 |
| 1 | e Arg Val Ala Val 80 Ser |
| 1 | Arg Val Val Val Ser Asp |
| 1 | Arg Val Val Val Ser Asp |
| 1 | e Arg Val Ala Val 80 Ser Asp |
| 1 | Arg Val Ala Val 80 Ser Asp Cys Thr |
| 1 | Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 |
| 1 | Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg |
| 1 | Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg |
| 1 | Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg |
| 1 | e Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg |

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225 230 <210> 19 <211> 378 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (378) <400> 19 atg agg tca gaa gag agg ccg ggt cac att gaa aag ttc cta aag agg 48 Met Arg Ser Glu Glu Arg Pro Gly His Ile Glu Lys Phe Leu Lys Arg 10 geg gac aag geg atc gac age geg gtc gag cag ggc gtc aag agg gcc 96 Ala Asp Lys Ala Ile Asp Ser Ala Val Glu Gln Gly Val Lys Arg Ala 25 gac gag ata cta gac gat gca gtc gag ctc ggc aag att acg gtg ggc 144 Asp Glu Ile Leu Asp Asp Ala Val Glu Leu Gly Lys Ile Thr Val Gly 40 gag gcg cag agg agg agc gat gtg ctg ctc aaa cag gcc gag cgg gag Glu Ala Gln Arg Arg Ser Asp Val Leu Leu Lys Gln Ala Glu Arg Glu 50 55 age agg egg etc aag tec aag gge gee aaa aag etc gaa aag gge ata 240 Ser Arg Arg Leu Lys Ser Lys Gly Ala Lys Lys Leu Glu Lys Gly Ile 65 gge gee gea aaa aag atg gea gea gge aag gge gae geg ete gag aeg 288 Gly Ala Ala Lys Lys Met Ala Ala Gly Lys Gly Asp Ala Leu Glu Thr 85 ctc gca aag ctc ggc gag ctc aga aag gcg ggg atc ata acg gag aaa 336 Leu Ala Lys Leu Gly Glu Leu Arg Lys Ala Gly Ile Ile Thr Glu Lys 105 100 gag ttt cgc gcc aaa aag aaa aag ctc ctc gca gag atc tga 378 Glu Phe Arg Ala Lys Lys Lys Leu Leu Ala Glu Ile * 120 115 <210> 20 <211> 125 <212> PRT <213> Cenarchaeum symbiosum <400> 20 Met Arg Ser Glu Glu Arg Pro Gly His Ile Glu Lys Phe Leu Lys Arg 10 Ala Asp Lys Ala Ile Asp Ser Ala Val Glu Gln Gly Val Lys Arg Ala 25 Asp Glu Ile Leu Asp Asp Ala Val Glu Leu Gly Lys Ile Thr Val Gly 40 Glu Ala Gln Arg Arg Ser Asp Val Leu Leu Lys Gln Ala Glu Arg Glu

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145

150

Ser Arg Arg Leu Lys Ser Lys Gly Ala Lys Lys Leu Glu Lys Gly Ile 70 75 Gly Ala Ala Lys Lys Met Ala Ala Gly Lys Gly Asp Ala Leu Glu Thr Leu Ala Lys Leu Gly Glu Leu Arg Lys Ala Gly Ile Ile Thr Glu Lys 105 Glu Phe Arg Ala Lys Lys Lys Leu Leu Ala Glu Ile 120 <210> 21 <211> 600 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(600) <400> 21 atg tee cag acg ggg gee eeg gge ggg cat gee tge acg eea tac acg 48 Met Ser Gln Thr Gly Ala Pro Gly Gly His Ala Cys Thr Pro Tyr Thr 5 cac gat cac gcc tcg atc gag ctc aag gac gcg tgg gcc tcg tcg agg 96 His Asp His Ala Ser Ile Glu Leu Lys Asp Ala Trp Ala Ser Ser Arg 25 aac gtc egc gag atg tac ttt gtg acc gcc acg ttc tcg tcc gag agc 144 Asn Val Arg Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Glu Ser cag ccg tac ttt gca ccg cag gcc aac cac tac ctg ctg gca agg ttc 192 Gln Pro Tyr Phe Ala Pro Gln Ala Asn His Tyr Leu Leu Ala Arg Phe aag gac gcc ccc aga atg atc aag gcg gtg ggc cgg ggg gag ggc gca 240 Lys Asp Ala Pro Arg Met Ile Lys Ala Val Gly Arg Gly Glu Gly Ala 65 70 tee tat gtg ttt age atg gae gag gae ata tte gag agg gag tee eec 288 Ser Tyr Val Phe Ser Met Asp Glu Asp Ile Phe Glu Arg Glu Ser Pro ggg gtg agc tat gta tcg gtg tac tat ctg gag tac ggc gat tcc gag 336 Gly Val Ser Tyr Val Ser Val Tyr Tyr Leu Glu Tyr Gly Asp Ser Glu 100 gag gac ata tgc gag gtg gcg tcc gtg gtg ggg aga aag gag aag ata 384 Glu Asp Ile Cys Glu Val Ala Ser Val Val Gly Arg Lys Glu Lys Ile 115 120 ggc agg gcg gga ata ggg cgc atg gac gtc tgc tcg agg gtg ccg cca 432 Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Val Pro Pro 135 aag tit goo tit oog tad age ggg aad ata ata gto oto gag gto too 480 Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Ile Val Leu Glu Val Ser

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age gag aag age tae eag age gte aae aag tae tge gag aag aeg egg 528 Ser Glu Lys Ser Tyr Gln Ser Val Asn Lys Tyr Cys Glu Lys Thr Arg ege gag gte ate ege aag ggg ata aeg atg ace aac ett gtg age etg Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val Ser Leu 180 tcc ata ctg gag cgg cta aag tag 600 Ser Ile Leu Glu Arg Leu Lys * 195 <210> 22 <211> 199 <212> PRT <213> Cenarchaeum symbiosum <400> 22 Met Ser Gln Thr Gly Ala Pro Gly Gly His Ala Cys Thr Pro Tyr Thr His Asp His Ala Ser Ile Glu Leu Lys Asp Ala Trp Ala Ser Ser Arq Asn Val Arg Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Glu Ser Gln Pro Tyr Phe Ala Pro Gln Ala Asn His Tyr Leu Leu Ala Arg Phe 55 Lys Asp Ala Pro Arg Met Ile Lys Ala Val Gly Arg Gly Glu Gly Ala Ser Tyr Val Phe Ser Met Asp Glu Asp Ile Phe Glu Arg Glu Ser Pro 90 Gly Val Ser Tyr Val Ser Val Tyr Tyr Leu Glu Tyr Gly Asp Ser Glu 105 Glu Asp Ile Cys Glu Val Ala Ser Val Val Gly Arg Lys Glu Lys Ile 120 Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Val Pro Pro 135 Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Ile Val Leu Glu Val Ser 155 150 Ser Glu Lys Ser Tyr Gln Ser Val Asn Lys Tyr Cys Glu Lys Thr Arg 170 Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val Ser Leu 180 185 Ser Ile Leu Glu Arg Leu Lys 195 <210> 23 <211> 810 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(810) <400> 23

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| 1 | | | | 5 | | | | | 10 |) | | | | 15 | i | |
|-------------------|-------------------|------------|--------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|-------------------|------------|-------------------|-------------------|-----|
| | | | | Val | | | | | Asp | | | | | Arg | ctg
Leu | 96 |
| | | | Arg | | | | | Ala | | | | | Ser | | ggc | 144 |
| ctg
Leu | cag
Gln
50 | Asn | ccg
Pro | ccc
Pro | gta
Val | ata
Ile
55 | cag
Gln | agg
Arg | ggc | ggc | agg
Arg
60 | Gly | ctg
Leu | tac
Tyr | ctg
Leu | 192 |
| | | | | | | | | | | | | cat
His | | | gca
Ala
80 | 240 |
| | | | | | | | | | | | | gag
Glu | | | | 288 |
| | | | | | | | | | | | | cac
His | | | | 336 |
| | | | | | | | | | | | | ctc
Leu
125 | | | | 384 |
| | | | | | | | | | | | | tcg
Ser | | | | 432 |
| ttc
Phe
145 | aaa
Lys | aag
Lys | tac
Tyr | cac
His | ggc
Gly
150 | ttt
Phe | gcg
Ala | ggc
Gly | gtg
Val | ccg
Pro
155 | gag
Glu | aag
Lys | atc
Ile | aag
Lys | gcg
Ala
160 | 480 |
| cta
Leu | gtc
Val | ccc
Pro | Gly
aaa | acc
Thr
165 | ata
Ile | tcc
Ser | cgg
Arg | gac
Asp | gag
Glu
170 | gcg
Ala | aca
Thr | aag
Lys | ctg
Leu | tac
Tyr
175 | cag
Gln | 528 |
| gcc
Ala | | | | | | | | | | | | | | | | 576 |
| agg
Arg | | | | | | Arg | | | | | | ctg
Leu
205 | | | | 624 |
| agc
Ser | ccc
Pro
210 | cgc
Arg | tcg
Ser | ggc
Gly | His | agg
Arg
215 | atc
Ile | ctg
Leu | cta
Leu | Lys | agg
Arg
220 | gtg
Val . | cgc
Arg | aag
Lys | acg
Thr | 672 |
| ggc
Gly
225 | | | | Lys | | | | | Leu | | | | | Ala . | | 720 |

Met Ala Arg Arg Tyr Lys Pro Arg Ile Lys Gln Val Leu Arg Glu Val Pro Leu Lys Asn Val His Val Trp Lys Asp Ala Gln Ala Arg Arg Leu 25 Asp Arg Ser Arg Val Arg Glu Ile Ala Lys Ser Ile Arg Ser Glu Gly 40 Leu Gln Asn Pro Pro Val Ile Gln Arg Gly Gly Arg Gly Leu Tyr Leu 55 Leu Ile Ser Gly Asn His Arg Leu Ala Ala Leu Lys His Leu Gly Ala 75 Lys Lys Ser Lys Phe Leu Val Ile Thr Lys Asp Thr Glu Tyr Gly Leu 90 Glu Asp Ala Lys Ala Ala Ser Val Val Glu Asn Leu His Arg Met Gln 105 Met Ser Pro Arg Glu Leu Ala Asp Ala Cys Arg Phe Leu Ala Glu Gln 120 Met Thr Arg Ala Glu Ala Ala Arg Lys Leu Gly Met Ser Met Pro Thr 140 135 Phe Lys Lys Tyr His Gly Phe Ala Gly Val Pro Glu Lys Ile Lys Ala 155 150 Leu Val Pro Gly Thr Ile Ser Arg Asp Glu Ala Thr Lys Leu Tyr Gln 170 165 Ala Val Pro Thr Val Ser Gln Ala Leu Lys Val Ala Leu Asn Ile Ser 185 Arg Leu Asp Arg Pro Ser Arg Arg Ile Tyr Leu Arg Leu Leu Ala Gln 205 200 Ser Pro Arg Ser Gly His Arg Ile Leu Leu Lys Arg Val Arg Lys Thr 220 215 Gly Val Arg Lys Lys Ile Pro Ile Glu Leu Gly Lys Asn Gly Ala Arg 230 235 Lys Leu Ala Arg Val Ala Glu Arg Glu Gly Thr Asp Glu Thr Arg Leu Ala Asn Arg Ile Val Arg Glu Tyr Leu Arg Lys Gln Arg

265

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<220>
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<222> (1)...(837)

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| | | 400 | 25 | | | | | | | | | | | | | | |
|------------|-----|-----|-----|-----|------------|-------------------|-----|-----|-----|------------|-----|-----|-----|-----|------------|----|-----|
| | tta | | gtg | | | | | | | Thr | | | | | aga
Arg | | 48 |
| | | | | Gln | | | | | Val | | | | | Ala | ccc
Pro | | 96 |
| | | | Ala | | | | | Cys | | | | | Pro | | gtc
Val | 1 | .44 |
| | | Ile | | | | | _ | | | _ | _ | | | _ | ata
Ile | 1 | .92 |
| | Asn | | | | | gag
Glu | | | | | | | | | | 2 | 40 |
| | | | - | | _ | Gly
aaa | - | _ | _ | | | | _ | | | 2 | 88 |
| | | | | | | cac
His | | | | | | | | | | 3 | 36 |
| | | | | | | cat
His | | | | | | | | | | | 84 |
| | | | | | | gag
Glu
135 | | | | | | | | | | 4: | 32 |
| Ala
145 | Ile | Ile | Asn | His | Ser
150 | gag
Glu | His | Arg | Val | Pro
155 | Ala | Asp | Gln | Val | Ala
160 | 41 | 80 |
| | | | | | | agg
Arg | | | | | | | | | | 52 | 28 |
| | | | | | | gcc
Ala | | | | | | | | | | 51 | 76 |
| | | | | | | ccc
Pro | | | | | | | | | | 62 | 24 |
| | | | | | Gln | gtc
Val
215 | | | | Ala | | | | | | 67 | 72 |
| 999 | gct | ggc | ggc | gta | aag | ctg | ctc | tgc | 999 | gcg | ggc | ata | acc | tcc | 999 | 72 | 0 |

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Gly Ala Gly Gly Val Lys Leu Leu Cys Gly Ala Gly Ile Thr Ser Gly 235 230 gcg gac gtg cgc agg gcc ctc gag ctt ggc tcc gag ggc att ctt gtg 768 Ala Asp Val Arg Arg Ala Leu Glu Leu Gly Ser Glu Gly Ile Leu Val 245 250 gea age ggg gte gta aag teg gea gae eee gea ggg gee ate ggg gag 816 Ala Ser Gly Val Val Lys Ser Ala Asp Pro Ala Gly Ala Ile Gly Glu 265 ctt gcc cgg gcc atg tcc tga 837 Leu Ala Arg Ala Met Ser * 275 <210> 26 <211> 278 <212> PRT <213> Cenarchaeum symbiosum <400> 26 Met Leu Thr Val Phe Gly Lys Phe Ile Thr Thr Ile Arg Leu Asp Arg Ala Val Pro Pro Gln Ala Pro Val His Val Leu Tyr Arg Ala Ala Pro Arg Gly Thr Ala Gly Thr Gly Gly Cys Arg Gly Gly Ile Pro Gly Val Asp Arg Ile Asn Thr Arg Gly Ala Ala Val Arg Ser Pro Val Leu Ile Ile Asn Cys Lys Asn Tyr Glu Glu Ala Ala Gly Gly Arg Ile Arg Gly 70 Leu Ala Asp Ala Ala Ala Gly Ala Ala Ala Arg Tyr Gly Val Arg Ile Ala Ile Ala Pro Pro Gln His Leu Leu Gly Ile Ile Ala Gly Arg Asp 105 Leu Gly Val Leu Ala Gln His Val Asp Asp Lys Gly Thr Gly Ser Thr 120 Thr Gly Tyr Val Val Pro Glu Leu Leu Lys Gln Ser Gly Val Ser Gly 135 140 Ala Ile Ile Asn His Ser Glu His Arg Val Pro Ala Asp Gln Val Ala 150 155 Gly Leu Val Pro Arg Leu Arg Gly Leu Gly Met Val Ser Val Val Cys 170 Val Arg Asp Pro Ala Glu Ala Ala Asp Leu Ser Arg Tyr Cys Pro Asp 185 Tyr Ile Ala Ile Glu Pro Pro Glu Leu Ile Gly Ser Gly Arg Ser Val 200 Ser Thr Glu Arg Pro Gln Val Ile Gln Glu Ala Ala Glu Ala Ile Arg Gly Ala Gly Gly Val Lys Leu Leu Cys Gly Ala Gly Ile Thr Ser Gly 230 235 Ala Asp Val Arg Arg Ala Leu Glu Leu Gly Ser Glu Gly Ile Leu Val 250 245 Ala Ser Gly Val Val Lys Ser Ala Asp Pro Ala Gly Ala Ile Gly Glu 260 265 Leu Ala Arg Ala Met Ser

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Cys Cys Met Tyr Asp Glu Ala Val Tyr Gly Gly Arg Cys Gly Tyr Ile 40

Lys Thr Pro Gly Met Arg Gly Arg Val Thr Val Phe Leu Ser Gly Lys

Met Ile Ser Val Gly Ala Ser Ser Val Arg Ala Ser Phe Ala Gln Leu 70 75

His Glu Ala Arg Leu His Leu Phe Arg Asn Gly Ala Ala Gly Gly

Cys Thr Arg Pro Val Val Arg Asn Met Val Ala Thr Val Asp Ala Gly 105

Arg Thr Val Pro Ile Asp Arg Ile Ser Ser Arg Ile Pro Gly Ala Val 120

Tyr Asp Pro Gly Ser Phe Pro Gly Met Ile Leu Lys Gly Leu Gly Ser 135

Cys Ser Phe Leu Val Phe Ala Ser Gly Lys Val Val Ile Ala Gly Ala 150 155

Arg Ser Pro Gly Glu Leu Tyr Arg Ser Ser Phe Asp Leu Leu Ala Arg 165 170

Leu Asn Gly Ala Gly Ala 180

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<213> Cenarchaeum symbiosum

<220>

<221> CDS

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gca aca tac gac agc cag gca ggg gcg gtc gtc ctc aag ttt tac gag 96 Ala Thr Tyr Asp Ser Gln Ala Gly Ala Val Val Leu Lys Phe Tyr Glu 20

eeg gaa tea caa aag ate gta cae tgg aeg gae aat aeg ggg eac aaq Pro Glu Ser Gln Lys Ile Val His Trp Thr Asp Asn Thr Gly His Lys.

ecc tac tgc tat acg agg cag ecc ecc tec gag ett ggg gag ett gaa 192 Pro Tyr Cys Tyr Thr Arg Gln Pro Pro Ser Glu Leu Gly Glu Leu Glu

ggc agg gag gat gtg cta gga acg gag cag gtc atg cgg cac gac ctg 240

| Gly
65 | _ | Glu | Asp | Val | Leu
70 | _ | Thr | Glu | Gln | Val
75 | | Arg | His | Asp | Leu
80 | • | |
|-----------|---|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|---|-------------------|-----|-----|------------|---|-----|
| | - | _ | _ | _ | Val | | _ | | _ | Ile | | | _ | _ | ccc
Pro | | 288 |
| | - | | | | | | _ | | - | _ | | cgc
Arg | | Ile | atg
Met | | 336 |
| _ | - | | _ | | - | | _ | | | | | tat
Tyr
125 | | | _ | | 384 |
| | | | | | | | | | | | | ggc
Gly | | | | | 432 |
| | _ | | - | _ | | | | _ | | - | _ | ctg
Leu | • | | _ | | 480 |
| | | | | | | | | | | | | gcg
Ala | | _ | | ! | 528 |
| | | _ | | | | | | | | _ | _ | ctc
Leu | | _ | | ! | 576 |
| | | | | | | | | | | | | gtg
Val
205 | _ | | | • | 524 |
| | | | | | _ | | _ | | | _ | | agg
Arg | _ | _ | | 6 | 572 |
| | | | | | | | | | | | | ttc
Phe | | | | 7 | 720 |
| _ | | _ | _ | | | | | | | | | ggt
Gly | - | | J - J | 7 | 768 |
| | | | | | | | | | | | | gcg
Ala | | _ | _ | 8 | 316 |
| | | | | | | Val | | | | | _ | gac
Asp
285 | _ | | - | 8 | 164 |
| | | | | | | | | | | | | gta
Val | | _ | | 9 | 12 |

| - | | | _ | | _ | _ | | _ | | - | _ | | | | gga
Gly
320 | 960 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------------|-----|-----|-------------------|------|
| | | | | | | | | | | | | tca
Ser | | | | 1008 |
| | _ | | | _ | _ | | _ | _ | | | | aac
Asn | _ | - | | 1056 |
| | | | | | | | | | | | | gtc
Val
365 | | | | 1104 |
| _ | | | | | _ | | - | | | - | | cac
His | _ | | _ | 1152 |
| _ | _ | | | | _ | | | | | | | ctc
Leu | _ | _ | - | 1200 |
| _ | | | | _ | _ | | - | | _ | | | gat
Asp | - | _ | | 1248 |
| | | | | | | | | | | | | tac
Tyr | | | | 1296 |
| _ | _ | - | | | | | _ | | | _ | | ctg
Leu
445 | | | | 1344 |
| _ | _ | | | _ | | _ | | _ | | _ | _ | aaa
Lys | _ | | _ | 1392 |
| | | | _ | _ | ~ ~ | | - | | | | | ttt
Phe | _ | _ | - | 1440 |
| | - | - | | | _ | _ | | | _ | | | aag
Lys | | | | 1488 |
| | _ | | | | _ | | _ | | | _ | _ | tgc
Cys | | _ | | 1536 |
| | | | - | | | | | _ | - | | | aac
Asn
525 | | | _ | 1584 |
| aca | tcg | atg | ata | atc | ggc | tcg | ctg | cgg | gac | ctg | cgc | gtc | aac | tat | tac | 1632 |

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| Thr | Ser
530 | | Ile | e Ile | e Gly | / Ser
535 | | ı Arg | J Asp |) Let | 1 Arg | | l Asr | тул | Tyr | |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| | Ser | | | | | Thr | | | | | ı Glı | | | | cag
Gln
560 | 1680 |
| | | | | | Gln | | | | | Val | | | | | tac
Tyr | 1728 |
| | | | | Ala | | | | | Leu | | | | | Ala | gca
Ala | 1776 |
| | | | | | | | | Tyr | | | | | Thr | | tcg
Ser | 1824 |
| | | gag
Glu | | | | | | | | | | Asp | | | | 1872 |
| | | ata
Ile | | | | | | | | | | | | | | 1920 |
| | | aag
Lys | | | | | | | | | | | | | | 1968 |
| | | gtc
Val | | | | | | | | | | | | | | 2016 |
| cgg
Arg | gca
Ala | ggc
Gly
675 | aag
Lys | gtc
Val | gac
Asp | gtc
Val | aag
Lys
680 | Gly
ggg | ctg
Leu | acg
Thr | ggc
Gly | aaa
Lys
685 | aag
Lys | tcg
Ser | cac
His | 2064 |
| acg
Thr | ccc
Pro
690 | ccg
Pro | ttc
Phe | ata
Ile | aag
Lys | gag
Glu
695 | ctc
Leu | ttc
Phe | tac
Tyr | tcg
Ser | ctg
Leu
700 | ctc
Leu | gac
Asp | ata
Ile | ctc
Leu | 2112 |
| tca
Ser
705 | gga
Gly | gtc
Val | gag
Glu | agc
Ser | gag
Glu
710 | gac
Asp | gag
Glu | ttc
Phe | gag
Glu | tca
Ser
715 | gcc
Ala | aag
Lys | atg
Met | agg
Arg | atc
Ile
720 | 2160 |
| tca
Ser | aag
Lys | gcg
Ala | Ile | gcc
Ala
725 | gcg
Ala | tgc
Cys | ggc
Gly | aag
Lys | agg
Arg
730 | ctc
Leu | gag
Glu | gag
Glu | agg
Arg | cag
Gln
735 | atc
Ile | 2208 |
| ccc
Pro | ctc
Leu | gtg
Val | gac
Asp
740 | ctg
Leu | gcg
Ala | ttc
Phe | aat
Asn | gtg
Val
745 | atg
Met | ata
Ile | agc
Ser | Lys | gcg
Ala
750 | ccc
Pro | tcc
Ser | 2256 |
| gaa
Glu | Tyr | gtc
Val
755 | aag :
Lys ' | acc
Thr | gtc
Val | Pro | cag
Gln
760 | cac
His | ata
Ile | cgg
Arg | Ala | gca
Ala
765 | agg
Arg | ctg
Leu | ctg
Leu | 2304 |

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gag aac gca agg gag gtc aaa aag ggc gac ata ata tcg tac gta aag 2352 Glu Asn Ala Arg Glu Val Lys Lys Gly Asp Ile Ile Ser Tyr Val Lys 775 gtg atg aac aag acc ggc gtc aag ccg gtg gag atg gcc cgg gca ggc 2400 Val Met Asn Lys Thr Gly Val Lys Pro Val Glu Met Ala Arg Ala Gly 790 795 gag gtg gac acg tca aag tac ctc gag ttc atg gag tcg acg ctc gac 2448 Glu Val Asp Thr Ser Lys Tyr Leu Glu Phe Met Glu Ser Thr Leu Asp 805 cag ctc acc tcg tcc atg ggc ctt gac ttt gac gag ata ctc ggc aag 2496 Gln Leu Thr Ser Ser Met Gly Leu Asp Phe Asp Glu Ile Leu Gly Lys 820 cca aag cag acc ggc atg gag cag ttc ttt ttc aaa tga 2535 Pro Lys Gln Thr Gly Met Glu Gln Phe Phe Lys * 835 <210> 30 <211> 844 <212> PRT <213> Cenarchaeum symbiosum <400> 30 Met Thr Val Gln Asp Ala Val Glu Ile Pro Pro Ser Leu Leu Val Ser Ala Thr Tyr Asp Ser Gln Ala Gly Ala Val Val Leu Lys Phe Tyr Glu 20 25 Pro Glu Ser Gln Lys Ile Val His Trp Thr Asp Asn Thr Gly His Lys Pro Tyr Cys Tyr Thr Arg Gln Pro Pro Ser Glu Leu Gly Glu Leu Glu 55 Gly Arg Glu Asp Val Leu Gly Thr Glu Gln Val Met Arg His Asp Leu Ile Ala Asp Lys Asp Val Pro Val Thr Lys Ile Thr Val Ala Asp Pro 90 Leu Ala Ile Gly Gly Thr Asn Ser Glu Lys Ser Ile Arg Asn Ile Met 105 Asp Thr Trp Glu Ser Asp Ile Lys Tyr Tyr Glu Asn Tyr Leu Tyr Asp 120 125 Lys Ser Leu Val Val Gly Arg Tyr Tyr Ser Val Ser Gly Gly Lys Val 135 Ile Pro His Asp Met Pro Ile Ser Asp Glu Val Lys Leu Ala Leu Lys 150 155 Ser Leu Leu Trp Asp Lys Val Val Asp Glu Gly Met Ala Asp Arg Lys 165 170 Glu Phe Arg Glu Phe Ile Ala Gly Trp Ala Asp Leu Leu Asn Gln Pro 185 Ile Pro Arg Ile Arg Arg Leu Ser Phe Asp Ile Glu Val Asp Ser Glu 200 205 Glu Gly Arg Ile Pro Asp Pro Lys Ile Ser Asp Arg Arg Val Thr Ala 215 220 Val Gly Phe Ala Ala Thr Asp Gly Leu Lys Gln Val Phe Val Leu Arg 230 235

Ser Gly Ala Glu Glu Glu Glu Asn Gly Val Thr Pro Gly Val Glu Val

| Val | Dhe | ጥህተ | Δen | 245 | Glu | Δla | Asp | Met | 250
Ile | | Asp | Ala | Leu | 255
Ser | |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|----------------|------------|------------|------------|------------|------------|------------|
| | | _ | 260 | - | | | | 265 | | | | | 270 | | |
| | _ | 275 | _ | | | | 280 | | | | | 285 | Asp | | _ |
| | 290 | | | | | 295 | | | | | 300 | | Ser | | |
| Двр
305 | Ile | Pro | Leu | Tyr | Met
310 | Met | Arg | qeA | Ser | Ala
315 | Thr | Leu | Arg | His | Gly
320 |
| Val | His | Leu | Asp | Leu
325 | Tyr | Arg | Thr | Phe | Ser
330 | Asn | Arg | Ser | Phe | Gln
335 | Leu |
| Tyr | Ala | Phe | Ala
340 | Ala | Lys | Tyr | Thr | Asp
345 | Tyr | Ser | Leu | Asn | Ser
350 | Val | Thr |
| Lys | Ala | Met
355 | Leu | Gly | Glu | Gly | Lys
360 | Val | qaA | Tyr | Gly | Val
365 | Lys | Leu | Gly |
| Asp | Leu
370 | Thr | Leu | Tyr | Gln | Thr
375 | Ala | Asn | Tyr | Cys | Tyr
380 | His | Asp | Ala | Arg |
| Leu
385 | Thr | Leu | Glu | Leu | Ser
390 | Thr | Phe | Gly | | Glu
395 | Ile | Leu | Met | Asp | Leu
400 |
| Leu | Val | Val | Thr | Ser
405 | Arg | Ile | Ala | Arg | Met
410 | Pro | Ile | Asp | Asp | Met
415 | Ser |
| Arg | Met | Gly | Val
420 | Ser | Gln | Trp | Ile | Arg
425 | Ser | Leu | Leu | Tyr | Tyr
430 | Glu | His |
| Arg | Gln | Arg
435 | Asn | Ala | Leu | Ile | Pro
440 | Arg | Arg | Asp | Glu | Leu
445 | Glu | Gly | Arg |
| Ser | Arg
450 | Glu | Val | Ser | Asn | Asp
455 | Ala | Val | Ile | Lys | Asp
460 | Lys | Lys | Phe | Arg |
| Gly
465 | Gly | Leu | Val | Val | Glu
470 | Pro | Glu | Glu | Gly | Ile
475 | His | Phe | Asp | Val | Thr
480 |
| Val | Met | Asp | Phe | Ala
485 | Ser | Leu | Tyr | Pro | Ser
490 | Ile | Ile | Lys | Val | Arg
495 | Asn |
| Leu | Ser | Tyr | Glu
500 | Thr | Val | Arg | Cys | Val
505 | His | Ala | Glu | Cys | Lys
510 | Lys | Asn |
| Thr | Ile | Pro
515 | Asp | Thr | Asn | His | Trp
520 | Val | Cys | Thr | Lys | Asn
525 | Asn | Gly | Leu |
| Thr | Ser
530 | Met | Ile | Ile | Gly | Ser
535 | Leu | Arg | Asp | Leu | Arg
540 | Val | Asn | Tyr | Tyr |
| Lys
545 | Ser | Leu | Ser | Lys | Ser
550 | Thr | Ser | Ile | Thr | Glu
555 | Glu | Gln | Arg | Gln | Gln
560 |
| Tyr | Thr | Val | Ile | Ser
565 | Gln | Ala | Leu | Lys | Val 570 | Val | Leu | Asn | Ala | Ser
575 | Tyr |
| Gly | Val | Met | Gly
580 | Ala | Glu | Ile | Phe | Pro
585 | Leu | Tyr | Phe | Leu | Pro
590 | Ala | Ala |
| Glu | Ala | Thr
595 | Thr | Ala | Val | Gly | Arg
600 | Tyr | Ile | Ile | Met | Gln
605 | Thr | Ile | Ser |
| His | Cys
610 | Glu | Gln | Met | Gly | Val
615 | Arg | Val | Leu | Tyr | Gly
620 | Asp | Thr | Ąsp | Ser |
| Leu
625 | Phe | Ile | Lys | Asp | Pro
630 | Glu | Glu | Arg | Gln | Ile
635 | His | Glu | Ile | Val | Glu
640 |
| His | Ala | Lys | Lys | Glu
645 | His | Gly | Val | Glu | Leu
650 | Glu | Val | Asp | Lys | Glu
655 | Tyr |
| Arg | Tyr | Val | Val
660 | Leu | Ser | Asn | Arg | Lys
665 | Lys | Asn | Tyr | Phe | Gly
670 | Val | Thr |
| Arg | Ala | Gly
675 | | Val | Asp | Val | Lys
680 | | Leu | Thr | Gly | Lys
685 | Lys | Ser | His |
| Thr | Pro
690 | | Phe | Ile | Lys | Glu
695 | | Phe | Tyr | Ser | Leu
700 | | Asp | Ile | Leu |
| Ser | | Val | Glu | Ser | Glu | | Glu | Phe | Glu | Ser | | Lys | Met | Arg | Ile |

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710 715 Ser Lys Ala Ile Ala Ala Cys Gly Lys Arg Leu Glu Glu Arg Gln Ile Pro Leu Val Asp Leu Ala Phe Asn Val Met Ile Ser Lys Ala Pro Ser 745 Glu Tyr Val Lys Thr Val Pro Gln His Ile Arg Ala Ala Arg Leu Leu 760 Glu Asn Ala Arg Glu Val Lys Lys Gly Asp Ile Ile Ser Tyr Val Lys Val Met Asn Lys Thr Gly Val Lys Pro Val Glu Met Ala Arg Ala Gly 790 795 Glu Val Asp Thr Ser Lys Tyr Leu Glu Phe Met Glu Ser Thr Leu Asp 810 Gln Leu Thr Ser Ser Met Gly Leu Asp Phe Asp Glu Ile Leu Gly Lys 825 Pro Lys Gln Thr Gly Met Glu Gln Phe Phe Lys <210> 31 <211> 555 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (555) <400> 31 atg ccg ggc ggg ggc agg ctg ccc gtg agc ggc ttt gag cgc cct acc 48 Met Pro Gly Gly Arg Leu Pro Val Ser Gly Phe Glu Arg Pro Thr tgg gat gaa tat ttc atg ctg cag gcg gag ctt gca aag ctc cga tcc 96 Trp Asp Glu Tyr Phe Met Leu Gln Ala Glu Leu Ala Lys Leu Arg Ser 20 aac tgt ata gtc cgc aag gtg ggg gcc gta ata gtg agg gac cac cgg 144 Asn Cys Ile Val Arg Lys Val Gly Ala Val Ile Val Arg Asp His Arg 40 cag ctc gcc aca ggg tat aac ggg acg cct cct ggc gtc aag aac tgc 192 Gln Leu Ala Thr Gly Tyr Asn Gly Thr Pro Pro Gly Val Lys Asn Cys tac gag ggc ggc tgc gag agg tgt gcc gag cgc atc gag ggc agg atc 240 Tyr Glu Gly Gly Cys Glu Arg Cys Ala Glu Arg Ile Glu Gly Arg Ile 65 70 aag tea gge gag gee etg gae egg tge etg tge aac eat gea gag gee 288 Lys Ser Gly Glu Ala Leu Asp Arg Cys Leu Cys Asn His Ala Glu Ala aac gct ata atg cac tgt gcg ata ctc ggg ata ggc gcg ggg ggc ggg 336 Asn Ala Ile Met His Cys Ala Ile Leu Gly Ile Gly Ala Gly Gly 100 ggg gcc acc atg tac acc acg ttc tcg ccg tgt ctg gag tgt acc aag 384 Gly Ala Thr Met Tyr Thr Thr Phe Ser Pro Cys Leu Glu Cys Thr Lys

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<221> CDS

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| | < | 400> | 33 | | | | | | | | | | | | | |
|------------|------------|------------------|------------|------------|------------|-------------------|------------------|------------|------------|------------|------------|------------------|------------|------------|------------|-----|
| | | | | | | acg
Thr | | | | | | | | | gtc
Val | 48 |
| | | | | | | gtg
Val | | | | | | | | | gag
Glu | 96 |
| aac
Asn | tgt
Cys | atc
Ile
35 | gtg
Val | gtg
Val | ctc
Leu | ccg
Pro | acg
Thr
40 | ggc
Gly | ctc
Leu | ggc
Gly | aag
Lys | act
Thr
45 | gcc
Ala | gtc
Val | gcc
Ala | 144 |
| | _ | | | _ | | tat
Tyr
55 | | | | | | | | | | 192 |
| | | | | | | ctg
Leu | | | | | | | | | | 240 |
| | | | | | | gat
Asp | | | | | | | | | | 288 |
| | | | | | | gcg
Ala | | | | | | | | | | 336 |
| | | | _ | _ | | gat
Asp | | | _ | | | | | | | 384 |
| | | | | | | ttc
Phe
135 | | | | | | | | | | 432 |
| | _ | | | Ser | | gcg
Ala | | | Val | | Asp | | | | | 480 |
| | | | | | | ctt
Leu | | | | | | | | | | 528 |
| | _ | | | - | | tcc
Ser | | | | | | | | | | 576 |
| | | | | | | tat
Tyr | | | | | | | | | | 624 |
| _ | | _ | | | | gag
Glu
215 | _ | _ | | | _ | | | | _ | 672 |
| ctg | gcc | ctc | gac | gag | agg | tat | tcc | tcc | ctc | aag | agg | tgc | 999 | tac | gat | 720 |

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| Leu
225 | | Leu | Asp | Glu | Arg
230 | - | Ser | Ser | Leu | Lys
235 | _ | Cys | Gly | туг | Asp
240 | |
|------------|-------------------|-----|-----|-----|------------|---|-----|-----|-----|------------|---|-----|-----|-----|------------|------|
| | ggc | | | | | | | | | Leu | | | | | | 768 |
| | ctt
Leu | | | | | _ | | _ | _ | _ | _ | | | | | 816 |
| _ | ata
Ile | _ | | | | | | | | _ | | | _ | - | | 864 |
| | cta
Leu
290 | | | | | | | | | | | | | | | 912 |
| | gag
Glu | _ | | _ | _ | _ | | | | | | _ | | ~ ~ | J . | 960 |
| _ | aag
Lys | - | | _ | | _ | | _ | | | | _ | | | _ | 1008 |
| | gag
Glu | - | _ | _ | _ | | _ | | | _ | | _ | - | | _ | 1056 |
| _ | tat
Tyr | - | - | | _ | _ | | | | | _ | | _ | - | _ | 1104 |
| | ata
Ile
370 | | | | | | | | | | | | _ | | | 1152 |
| | cag
Gln | | | | | | | | | | | | | | | 1200 |
| | gac
Asp | | | | | | | | | | | | | | | 1248 |
| | gag
Glu | | | | | | | | | | | | | | | 1296 |
| | tac
Tyr | | | | | | | | | | | | | | | 1344 |
| | ata
Ile
450 | | | | Ala | | | | | Asp | | | | | | 1392 |

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att ggt cgg cgc aag atg agc gcc gcc aag ggc atg ggt gag agg atg 1440 Ile Gly Arg Arg Lys Met Ser Ala Ala Lys Gly Met Gly Glu Arg Met 475 470 aac egg teg etg geg gea gge ggt get get gee aag gee get eea aag 1488 Asn Arg Ser Leu Ala Ala Gly Gly Ala Ala Ala Lys Ala Ala Pro Lys 490 1509 gga ctc gag ggg tac ttt tag Gly Leu Glu Gly Tyr Phe * 500 <210> 34 <211> 502 <212> PRT <213> Cenarchaeum symbiosum Met Glu Thr Gly His Ile Thr Gly Arg Tyr Ile Glu Pro Gly Ala Val 10 Glu Arg Arg Asp Tyr Gln Val Gly Leu Ala Glu Gln Ala Ile Arg Glu 25 Asn Cys Ile Val Val Leu Pro Thr Gly Leu Gly Lys Thr Ala Val Ala 40 Leu Gln Val Ile Ala His Tyr Leu Asp Glu Gly Arg Gly Ala Leu Phe 55 Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly 75 70 Arg Ala Leu Thr Ile Ser Asp Ile Thr Leu Val Thr Gly Glu Asp Thr 90 Ile Pro Arg Arg Lys Lys Ala Trp Gly Gly Ser Val Ile Cys Ala Thr 100 105 Pro Glu Ile Ala Arg Asn Asp Ile Glu Arg Gly Leu Val Pro Leu Glu 120 125 Gln Phe Gly Leu Val Ile Phe Asp Glu Ala His Arg Ala Val Gly Asp 135 Tyr Ala Tyr Ser Ser Ile Ala Arg Ala Val Gly Asp Asn Ser Arg Met 150 155 Val Gly Met Thr Ala Thr Leu Pro Ser Glu Arg Glu Lys Ala Asp Glu 165 170 Ile Met Gly Thr Leu Leu Ser Arg Ser Ile Ala Gln Arg Thr Glu Asp 185 Asp Pro Asp Val Lys Pro Tyr Val Glu Glu Thr Ala Thr Glu Trp Ile 200 Lys Val Asp Leu Pro Pro Glu Met Lys Glu Ile Gln Arg Leu Leu Lys 215 Leu Ala Leu Asp Glu Arg Tyr Ser Ser Leu Lys Arg Cys Gly Tyr Asp 235 230 Leu Gly Ser Asn Arg Ser Leu Ser Ala Leu Leu Arg Leu Arg Met Val 250 Val Leu Gly Gly Asn Arg Arg Ala Ala Lys Pro Leu Phe Thr Ala Ile 265 270 Arg Ile Thr Tyr Ala Leu Asn Ile Phe Glu Ala His Gly Val Thr Pro 280 285 Phe Leu Lys Phe Cys Glu Arg Thr Ser Lys Lys Gly Val Gly Val 295 300

Ala Glu Leu Phe Glu Gln Asp Arg Asn Phe Thr Gly Ala Ile Ala Arg

315

-85-

310

305

| בומ | | | | | 310 | | | | | 315 | | | | | 320 | |
|---|--|--|--|---|---|---|--|--|---|--|--|---|--|--|--|-------------------------|
| 7,24 | Lys | Ala | Ala | Gln
325 | Ala | Ala | Gly | Met | Glu
330 | His | Pro | Lys | Ile | Pro
335 | Lys | |
| Leu | Glu | Asp | Ala
340 | Val | Arg | Gly | Ala | Arg
345 | Gly | Lys | Ala | Leu | Val
350 | Phe | Thr | |
| Ser | Tyr | Arg
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| Gly | Ile
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| Lys
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390 | | Thr | Val | Ala | Lys
395 | | Arg | Asp | Gly | Gly
400 | |
| | Asp | Val | Leu | Val
405 | | Thr | Arg | Val | Gly
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415 | | |
| Ser | Glu | Val | Asn
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425 | | Asn | Val | Pro | Ser | | Ile | |
| Arg | Tyr | Val | Gln | Arg | Arg | Gly | Arg | | Gly | Arg | Lys | Asp
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| Leu | Ile
450 | | Leu | Met | Ala | Lys
455 | | Thr | Ile | Asp | Glu
460 | | Tyr | Tyr | Trp | |
| Ile
465 | | Arg | Arg | Lys | Met | | Ala | Ala | Lys | Gly
475 | | Gly | Glu | Arg | Met
480 | |
| | Arg | Ser | Leu | | | Gly | Gly | Ala | | | Lys | Ala | Ala | | | |
| Gly | Leu | Glu | Gly | 485
Tyr | Phe | , | | | 490 | | | | | 495 | | |
| | _ | | 500 | | | | | | | | | | | | | |
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21> | | | ream | Synu | 71050 | | | | | | | | | |
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tcg
Ser | CDS (1). 35 tac | ttt
Phe
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Thr | ata
Ile | aag
Lys | acc
Thr | Ala
10 | Asn | Leu | Ala | Leu | Pro
15 | Asp | |
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Phe
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Thr | ata
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Lys
gtc | acc
Thr | Ala
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tgc | Leu | Ala | Leu | Pro
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gtg | Asp | 48
96 |
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Phe
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tac
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Asn | ata
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His | aag
Lys
gtc
Val | acc
Thr
ctg
Leu
25 | Ala
10
gca
Ala | Asn
tgc
Cys | Leu
aag
Lys | Ala
agc
Ser | gag
Glu
30 | Pro
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gtg
Val | Asp
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Tyr | acc
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Lys
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Ile
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His | aag
Lys
gtc
Val
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Thr
40 | acc
Thr
ctg
Leu
25
tcc
Ser | Ala
10
gca
Ala
atc | tgc
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tcc
Ser | Leu
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Lys
tcg
Ser | agc
Ser
tct
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45 | gag
Glu
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<2
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Glu
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atc
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Ile
cac
His
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ctg
Leu
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Ala
atc
Ile | tgc
Cys
tcc
Ser | Leu
aag
Lys
tcg
Ser | agc
ser
tct
ser
45 | gag
Glu
30
agc
Ser | gtg
Val
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Gly | atg
Met
ctc
Leu | 96
144 |
| Met 1 gtg Val agg Arg | <2
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tca
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Ala | 221>
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Ser
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Lys
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Glu
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aac
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atc
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Ile
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Lys
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Val
acg
Thr
40 | acc
Thr
ctg
Leu
25
tcc
Ser | Ala
10
gca
Ala
atc
Ile | tgc
Cys
tcc
Ser | Leu
aag
Lys
tcg
Ser | agc
ser
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ser
45 | gag
Glu
30
agc
Ser | gtg
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Gly | atg
Met
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Leu | 96
144 |
| Met 1 gtg Val agg Arg gac Asp | <2
<4
tca
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gtc
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gcc
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aag
Lys | 221>
222>
100>
tcg
Ser
aaa
Lys
gag
Glu
35
tac | CDS (1) 35 tac Tyr aag Lys 20 aag Lys tcg Ser | ttt Phe 5 tac Tyr cag Gln gag | acc
Thr
aac
Asn
atc
Ile
ctc
Leu | ata
Ile
cac
His
cag
Gln
aag
Lys
55 | aag
Lys
gtc
Val
acg
Thr
40
caa
Gln | acc
Thr
ctg
Leu
25
tcc
Ser
cag
Gln | Ala
10
gca
Ala
atc
Ile
ttc | tgc
Cys
tcc
Ser
aac | Leu
aag
Lys
tcg
Ser
tcc | agc
ser
tct
ser
45
cgg
Arg | gag
Glu
30
agc
Ser
ata
Ile | Pro
15
gtg
Val
999
Gly
acc | atg
Met
ctc
Leu
gag
Glu | 96
144
192 |
| Met 1 gtg Val agg Arg gac Asp | <2
<2
tca
ser
gtc
Val
gcc
Ala
aag
Lys
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222>
100>
tcg
ser
aaa
Lys
gag
Glu
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tac
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Thr
aac
Asn
atc
Ile
ctc
Leu | ata
Ile
cac
His
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Gln
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Lys
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Lys
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Val
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Thr
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Gln | acc
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ttc
Phe | tgc
Cys
tcc
Ser
aac
Asn | Leu aag Lys tcg Ser tcc Ser 60 | Ala
agc
ser
tct
ser
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cgg
Arg | gag
Glu
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15
gtg
Val
ggg
Gly
acc
Thr | atg
Met
ctc
Leu
gag
Glu | 96
144 |
| Met 1 gtg Val agg Arg gac Asp | <2
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Val
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Ala
aag
Lys
50 | 221>
222>
100>
tcg
ser
aaa
Lys
gag
Glu
35
tac
Tyr | CDS (1). 35 tac Tyr aag Lys 20 aag Lys tcg Ser | ttt Phe 5 tac Tyr cag Gln gag Glu ata | acc
Thr
aac
Asn
atc
Ile
ctc
Leu | ata
Ile
cac
His
cag
Gln
aag
Lys
55 | aag
Lys
gtc
Val
acg
Thr
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caa
Gln | acc
Thr
ctg
Leu
25
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Ser
cag
Gln | Ala
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gca
Ala
atc
Ile
ttc
Phe | tgc
Cys
tcc
Ser
aac
Asn | Leu aag Lys tcg Ser tcc Ser 60 | Ala
agc
ser
tct
ser
45
cgg
Arg | gag
Glu
30
agc
Ser
ata
Ile | pro
15
gtg
Val
ggg
Gly
acc
Thr | atg
Met
ctc
Leu
gag
Glu | 96
144
192 |
| Met 1 gtg Val agg Arg gac Asp ttc Phe 65 | <2
<2
<4
tca
Ser
gtc
Val
gcc
Ala
aag
Lys
50
tac
Tyr | 221>
222>
100>
tcg
Ser
aaa
Lys
gag
Glu
35
tac
Tyr | CDS (1). 35 tac Tyr aag Lys 20 aag Lys tcg Ser tcg Ser | ttt Phe 5 tac Tyr cag Gln gag Glu ata Ile | acc
Thr
aac
Asn
atc
Ile
ctc
Leu
gaa
Glu
70 | ata
Ile
cac
His
cag
Gln
aag
Lys
55
gag
Glu | aag
Lys
gtc
Val
acg
Thr
40
caa
Gln
ctg
Leu | acc
Thr
ctg
Leu
25
tcc
Ser
cag
Gln
gaa
Glu | Ala
10
gca
Ala
atc
Ile
ttc
Phe | tgc
Cys
tcc
Ser
aac
Asn | aag
Lys
tcg
Ser
tcc
Ser
60 | agc
ser
tct
ser
45
cgg
Arg | gag
Glu
30
agc
Ser
ata
Ile
gtg
Val | gtg
val
ggg
Gly
acc
Thr | atg
Met
Ctc
Leu
gag
Glu
aag
Lys
80 | 96
144
192
240 |
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Thr
aac
Asn
atc
Ile
ctc
Leu
gaa
Glu
70
ctg | ata
Ile
cac
His
cag
Gln
aag
Lys
55
gag
Glu
ctg | aag
Lys
gtc
Val
acg
Thr
40
caa
Gln
ctg
Leu | acc
Thr
ctg
Leu
25
tcc
Ser
cag
Gln
gaa
Glu | Ala 10 gca Ala atc Ile ttc Phe aag Lys | tgc
Cys
tcc
Ser
aac
Asn
acc
Thr
75 | Leu aag Lys tcg Ser tcc Ser 60 ggt Gly | Ala agc ser tct ser 45 cgg Arg gcg Ala | gag
Glu
30
agc
Ser
ata
Ile
gtg
Val | gtg
val
ggg
Gly
acc
Thr
gtc
val | atg
Met
ctc
Leu
gag
Glu
aag
Lys
80 | 96
144
192 |

-86-85 90 95 gac atc tgg ctg tgc tgg aag aca ggc gag cgc gag atc aag ttc tgg 336 Asp Ile Trp Leu Cys Trp Lys Thr Gly Glu Arg Glu Ile Lys Phe Trp 100 cat gaa aag gac tet ggt ttt gge gga aga aag eee ata gag gta agt 384 His Glu Lys Asp Ser Gly Phe Gly Gly Arg Lys Pro Ile Glu Val Ser 115 120 gac gag tca cta gtg tag 402 Asp Glu Ser Leu Val * 130 <210> 36 <211> 133 <212> PRT <213> Cenarchaeum symbiosum <400> 36 Met Ser Ser Tyr Phe Thr Ile Lys Thr Ala Asn Leu Ala Leu Pro Asp Val Val Lys Lys Tyr Asn His Val Leu Ala Cys Lys Ser Glu Val Met 20 25 Arg Ala Glu Lys Gln Ile Gln Thr Ser Ile Ser Ser Ser Ser Gly Leu 40 Asp Lys Tyr Ser Glu Leu Lys Gln Gln Phe Asn Ser Arg Ile Thr Glu 55 60 Phe Tyr Arg Ser Ile Glu Glu Leu Glu Lys Thr Gly Ala Val Lys 70 Ser Ile Asp Glu Gly Leu Leu Asp Phe Pro Ala Lys Arg Phe Gly Asp 90 Asp Ile Trp Leu Cys Trp Lys Thr Gly Glu Arg Glu Ile Lys Phe Trp 105 His Glu Lys Asp Ser Gly Phe Gly Gly Arg Lys Pro Ile Glu Val Ser 120 115 Asp Glu Ser Leu Val 130 <210> 37 <211> 879 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(879) <400> 37 atg etc tee gee tgg ttg ege gta ata ege gte ege tte etg etc geg 48 Met Leu Ser Ala Trp Leu Arg Val Ile Arg Val Arg Phe Leu Leu Ala 5 96 Ser Val Ile Ala Val Ser Ala Gly Leu Ala Leu Ser Trp Trp His Gly

cac gaa ata gac gca ttc tcc gcc gcg ctc acc atg gcc ggc gtg gcc

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| His | Glu | Ile
35 | _ | Ala | Phe | Ser | Ala
40 | | Leu | Thr | Met | Ala
45 | | Val | Ala | |
|-----|-----|-----------|---|-----|-----|-----|-----------|---|-----|-----|-----|-------------------|---|-----|------------------|-----|
| | | His | - | | | | | | | | | Ser | | | aag
Lys | 192 |
| _ | | | - | | | | _ | | | _ | Met | _ | | | aca
Thr
80 | 240 |
| | | _ | | _ | | _ | | | | | _ | gtg
Val | | _ | - | 288 |
| | | | _ | - | _ | _ | | | | | | gcg
Ala | | | | 336 |
| | | | | | | | | | | | | ttt
Phe
125 | | | | 384 |
| - | | | | | _ | - | | | _ | _ | _ | ggc
Gly | | | | 432 |
| _ | | | _ | _ | _ | | _ | _ | | _ | | ggc
Gly | _ | | | 480 |
| | _ | | | _ | | _ | | - | - | - | _ | gtg
Val | | _ | _ | 528 |
| | | _ | | _ | _ | | _ | | | | | tcg
Ser | | | _ | 576 |
| | | | | _ | | | | | | | | gtt
Val
205 | | | - | 624 |
| | | | | | | | | | | | | ccc
Pro | | | | 672 |
| | | | | | | | | | | | | ctg
Leu | | | | 720 |
| | | | | | | | | | | | | att
Ile | | | | 768 |
| | | | | | | | | | | | | cgg
Arg | | | | 816 |

WO 00/18909 PCT/US99/22752 -88-

ggc acg ctg cgg ttt agc agg gtt gca ggc gcc ctg ctg gtg ttg ggc 864 Gly Thr Leu Arg Phe Ser Arg Val Ala Gly Ala Leu Leu Val Leu Gly 275 280 att ctg ttg ggc tga 879 Ile Leu Leu Gly * 290 <210> 38 <211> 292 <212> PRT <213> Cenarchaeum symbiosum <400> 38 Met Leu Ser Ala Trp Leu Arg Val Ile Arg Val Arg Phe Leu Leu Ala Ser Val Ile Ala Val Ser Ala Gly Leu Ala Leu Ser Trp Trp His Gly 25 His Glu Ile Asp Ala Phe Ser Ala Ala Leu Thr Met Ala Gly Val Ala 40 Ala Leu His Ala Ser Val Asp Met Leu Asn Asp Tyr Ser Asp Tyr Lys 55 Arg Gly Ile Asp Thr Ile Thr Lys Arg Thr Pro Met Ser Gly Gly Thr 70 75 Gly Val Leu Pro Glu Gly Leu Leu Thr Pro Gly Gln Val His Arg Ala 90 Gly Ile Ile Ser Leu Val Leu Gly Ser Ala Val Gly Ala Tyr Phe Val 105 Val Thr Thr Gly Pro Val Ile Ala Met Ile Leu Gly Phe Ala Val Val 120 Ser Ile Tyr Phe Tyr Ser Thr Arg Ile Val Asp Ser Gly Leu Ser Glu Val Phe Val Ala Val Lys Gly Ala Met Ile Val Leu Gly Ala Tyr Tyr 150 155 Ile Gln Ala Pro Glu Ile Thr Pro Ala Ala Val Leu Val Gly Ala Ala 170 Val Gly Ala Leu Ser Ser Ala Val Leu Phe Val Ala Ser Phe Pro Asp 185 His Asp Ala Asp Lys Ser Arg Gly Arg Lys Thr Leu Val Ile Ile Leu 200 Gly Lys Glu Arg Ala Ser Arg Ile Leu Trp Val Phe Pro Ala Val Ala 215 220 Tyr Ser Ser Val Ile Thr Gly Val Ile Leu Gln Phe Leu Pro Val His 230 235 Ala Leu Thr Met Leu Leu Ala Ala Pro Leu Ala Val Ile Ala Ala Lys 245 250 Gly Leu Ala Arg Glu Tyr Gly Gly Asp Gly Ile Ile Arg Val Met Arg 265 Gly Thr Leu Arg Phe Ser Arg Val Ala Gly Ala Leu Leu Val Leu Gly 275 280 Ile Leu Leu Gly 290 <210> 39 <211> 1119 <212> DNA <213> Cenarchaeum symbiosum

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| | < | :220>
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| | ato | | 999 | | | | | | | Thr | | | | | gag
Glu | 48 |
| | | | | His | | | | | | | | | | Leu | cac
His | 96 |
| | | aac
Asn
35 | | | | | | Tyr | | | | | | | | 144 |
| | | agg
Arg | | | | | | | | | | | | | | 192 |
| | | gtc
Val | | | | | | | | | | | | | | 240 |
| | | gtc
Val | | | | | | | | | | | | | | 288 |
| | | gac
Asp | | | | | | | | | | | | | | 336 |
| | | gag
Glu
115 | | | | | | | | | | | | | | 384 |
| | | ggc
Gly | | | | | | | | | | | | | | 432 |
| tgc
Cys
145 | atg
Met | aag
Lys | ccc
Pro | gcc
Ala | tat
Tyr
150 | cta
Leu | gag
Glu | gac
Asp | cag
Gln | ctg
Leu
155 | aag
Lys | agg
Arg | agc
Ser | ctt
Leu | gca
Ala
160 | 480 |
| | | ggc
Gly | | | | | | | | | | | | | | 528 |
| gag
Glu | | Gln | | | | | | | | | | | | | | 576 |
| gga
Gly | gag
Glu | gcc
Ala
195 | ttt
Phe | gcc
Ala | atg
Met | Tyr | gag
Glu
200 | aag
Lys | gca
Ala | agg
Arg | gag
Glu | gat
Asp
205 | ggc
Gly | cgc
Arg | atc
Ile | 624 |

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| | | | | | | | | | | | | gtt
Val | | | | 672 |
|----------|-----------|--------------|------------|----------|-----|-----------|-----------|-----------|-----------|-----|-----------|-------------------|-----------|-----------|-----|------|
| | _ | | | _ | _ | | _ | - | _ | - | - | aag
Lys | _ | | _ | 720 |
| | | | | | | | | | | | | ctg
Leu | | | | 768 |
| | | | | | | | | | | | | acg
Thr | | | | 816 |
| | | | | | | | | | | | | ggc
Gly
285 | | | | 864 |
| | _ | _ | | _ | | | | | | | | gag
Glu | | | | 912 |
| _ | _ | | | | | | | | _ | _ | _ | tcc
Ser | _ | _ | | 960 |
| | | | | | | | | | | | | Gly
ggg | | | | 1008 |
| | | | | | | | | | | | | gtg
Val | | | | 1056 |
| _ | | _ | _ | | | | | | | | | acc
Thr
365 | | | | 1104 |
| | | _ | aaa
Lys | _ | | | | | | | | | | | | 1119 |
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?13> | | rcha | eum | symb | oiosu | ım | | | | | | | | |
| Met
1 | | 00>
Ser | | His
5 | Ala | Thr | Ala | Glu | Gly
10 | Thr | Arg | Arg | Ile | Ala
15 | Glu | |
| • | Ser | Gly | Ala
20 | His | Ile | Asp | Asn | Tyr
25 | Lys | Met | Val | qaA | Gly
30 | | His | |
| Leu | Ser | Asn
35 | | Gly | Met | Gly | Thr
40 | | Leu | Gly | Asp | Ala
45 | | Asp | Ala | |
| Thr | Asp
50 | Arg | Ala | Val | Thr | Asp
55 | Ala | Val | Lys | Arg | Ser
60 | Val | Lys | Thr | Gly | |

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20

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Ile Asn Val Ile Asp Thr Ala Ile Asn Tyr Arg Leu Gln Arg Ala Glu
                     70
Arg Ser Val Gly Arg Ala Val Thr Glu Leu Ser Glu Glu Gly Leu Val
Ser Arg Asp Gln Ile Phe Ile Ser Thr Lys Ala Gly Tyr Val Thr Asn
                                105
Asp Ser Glu Val Ser Leu Asp Phe Trp Glu Tyr Val Lys Lys Glu Tyr
                            120
                                                125
Val Gly Gly Val Ile Gln Ala Gly Asp Ile Ser Ser Gly Tyr His
                        135
Cys Met Lys Pro Ala Tyr Leu Glu Asp Gln Leu Lys Arg Ser Leu Ala
                    150
                                        155
Asn Met Gly Leu Asp Cys Ile Asp Leu Val Tyr Val His Asn Pro Val
                165
                                    170
Glu Gly Gln Ile Lys Asp Arg Pro Ile Pro Glu Ile Leu Asp Cys Ile
                                185
Gly Glu Ala Phe Ala Met Tyr Glu Lys Ala Arg Glu Asp Gly Arg Ile
                            200
Arg Tyr Tyr Gly Leu Ala Thr Trp Glu Cys Phe Arg Val Ala Gly Asp
                        215
Asn Pro Gln Asn Val Gln Leu Glu Asp Val Val Lys Lys Ala Lys Asp
                    230
                                        235
Ala Gly Gly Asp Asn His Gly Phe Lys Phe Ile Gln Leu Pro Phe Asn
                                    250
Gln Tyr Phe Asp Gln Ala Tyr Met Leu Lys Asn Gln Thr Val Asp Gly
                                265
Arg Lys Leu Ser Ile Leu Asp Ala Ala Val Ser Leu Gly Val Gly Val
                            280
Phe Thr Ser Val Pro Phe Met Gln Gly Lys Leu Leu Glu Pro Gly Leu
                                            300
                        295
Leu Pro Glu Phe Gly Gly Leu Ser Pro Ala Leu Arg Ser Leu Gln Phe
                    310
                                        315
Ile Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro Gly His Asn Ser
                                   330
Ala Ala His Thr Asp Glu Asn Leu Lys Ile Met Gly Val Pro Pro Ile
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Pro Pro Asp Lys Phe Gly Glu Leu Val Ala Ser Leu Thr Ser Trp Ser
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                            360
Pro Gly Gln Lys
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                                                                      48
Met Ala Arg Gly Pro Ile Leu Ser Glu Lys Phe Gln Ile Leu Gln Gly
gac gcc cgg gag gtg ctg ccg cgg ctg gca aag aat aca gcc gag cqc
                                                                       96
Asp Ala Arg Glu Val Leu Pro Arg Leu Ala Lys Asn Thr Ala Glu Arg
```

25

| | | | Arg | _ | | - | | Ser | | | | tac
Tyr
45 | | | aga
Arg | 14 | . 4 |
|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|------------|-------------------|-----|-----|------------|-----|------------|
| _ | | | _ | | | | | _ | | _ | _ | aag
Lys | _ | | _ | 19 | 2 |
| | | | | | _ | - | | _ | | _ | Ser | tgc
Cys | _ | _ | _ | 24 | 0 |
| | | | | | | | | | | | | gat
Asp | | | | 28 | В |
| | _ | | - | _ | _ | _ | _ | | | | - | cta
Leu | | - | | 336 | 5 |
| | | | | | | | | | | | | tac
Tyr
125 | _ | _ | | 384 | 1 |
| _ | | _ | | - | _ | | | | _ | _ | _ | gcg
Ala | | _ | | 432 | 2 |
| | | | | | | | | | | | | gac
Asp | | | | 480 |) |
| | | _ | _ | | | | _ | _ | _ | | | aac
Asn | _ | | | 528 | ţ |
| | | | | | | | | | | | | gat
Asp | | | _ | 576 | i |
| | | | | | | Val | | | | | | Pro
205 | | | | 624 | |
| Phe | Asp
210 | Glu | Leu | Pro | Thr | Thr
215 | Gly | Glu | Ile | Ser | Trp
220 | gcc
Ala | His | Gly | Tyr | 672 | |
| | | | | | | | | | Tyr | | | ttc
Phe | | | | 720 | |
| | | | Lys | | | | | | | | | ccg
Pro | Ile | | | 768 | |
| gca | tgc | aac | ccg | cgg | ggc | aag | aac | ccg | 999 | aac | gtc | tgg | gag | ata | tcc | 816 | |

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| Ala | Cys | Asn | Pro
260 | Arg | Gly | Lys | Asn | Pro
265 | Gly | Asn | Val | Trp | Glu
270 | Ile | Ser | |
|----------|-----|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-------------------|------------|-----|-----|------|
| | - | | | | | | | | | | | ttc
Phe
285 | | | | 864 |
| | | | | | | | | | | | | ggc
Gly | | | | 912 |
| | | | | | | | | | | | | gtc
Val | | | | 960 |
| | | | | | | | | _ | _ | | | gcc
Ala | | | - | 1008 |
| | | | | | | | | | | | | cgg
Arg | | | | 1056 |
| _ | | | _ | _ | | _ | | ~ ~ | | _ | _ | acc
Thr
365 | | | | 1104 |
| tga
* | | | | | | | | | | | | | | | | 1107 |
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<211> 368

<212> PRT

<213> Cenarchaeum symbiosum

<400> 42

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Ala Asn Asp Arg Leu Gln Phe Ala Pro Gly Lys Arg Asp Pro Glu Ala 180 185 Ile Gly Arg Ile Ala Ala Val Ile His Gly Ser Thr Pro Gly Thr Pro 200 Phe Asp Glu Leu Pro Thr Thr Gly Glu Ile Ser Trp Ala His Gly Tyr 215 Asp Pro Glu Lys Tyr Cys Pro Thr Cys Tyr Arg Lys Phe Arg Arg His 230 235 Ala Thr Arg Lys Arg Ile Gly Gly His Glu His Tyr Pro Ile Phe Ala 250 Ala Cys Asn Pro Arg Gly Lys Asn Pro Gly Asn Val Trp Glu Ile Ser 260 265 Thr Lys Ala His His Gly Asn Glu His Phe Ala Val Phe Pro Glu Asp 275 280 285 Leu Val Ser Arg Ile Val Lys Phe Ala Thr Lys Glu Gly Asp Tyr Val 295 Leu Asp Pro Phe Ala Gly Arg Gly Thr Thr Gly Ile Val Ser Ala Cys 310 315 Leu Lys Arg Gly Phe Thr Gly Ile Asp Leu Tyr Pro Ala Asn Val Ala Arg Ala Arg Arg Asn Val Gln Asp Ser Ala Asp Ser Arg Leu Ser Lys 340 345 Lys Val Leu Asp Gln Ile Met Pro Glu Arg Gln Leu Thr Gly Tyr Phe 360 <210> 43 <211> 933 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(933) <400> 43 atg cet agt tae gea gaa ata gea aac gae gta ett ega eta atg gaq 48 Met Pro Ser Tyr Ala Glu Ile Ala Asn Asp Val Leu Arg Leu Met Glu tca gtc ggt gag cag gca cct ggt gta gta ctt cac gac tat ctt tca 96 Ser Val Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr Leu Ser 20 aaa ttg caa cag tat tcg ggg agg gat aca ata ctg tat gcg acc aac 144 Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala Thr Asn 35 tgg ata acg gac gaa gcg cat acg tct aat gaa gct ctc ata aca aat 192 Trp Ile Thr Asp Glu Ala His Thr Ser Asn Glu Ala Leu Ile Thr Asn 50 55 ggt gac ctg tat gga ttt atg agg atg atg cgt gat tta aaq act aaq 240 Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys Thr Lys 70 aaa tta gat tta ata ctc cac agt ccg ggg ggc tcc gtc gag tcc acc 288 Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Val Glu Ser Thr

| _ | _ | | - | | | | _ | _ | Lys | | | | _ | | atc
Ile | 336 |
|-------------------|---|---|---|---|---|-------------------|---|---|-----|---|-----|---|---|---|------------|-----|
| | | | | _ | | _ | _ | _ | _ | | _ | | _ | _ | tca
Ser | 384 |
| _ | | _ | _ | - | _ | ggt
Gly
135 | | | | _ | | | | | _ | 432 |
| | | | | | | acc
Thr | | | | _ | | | _ | | _ | 480 |
| - | | | | _ | | ttt
Phe | | | - | _ | _ | | | - | | 528 |
| | _ | | | | | gca
Ala | | | | - | | | | | | 576 |
| | | | | | | tgc
Cys | | | - | - | _ | | _ | | _ | 624 |
| | _ | | | | _ | gct
Ala
215 | _ | | _ | | | | | | _ | 672 |
| | _ | | _ | | | aaa
Lys | | | | | - | | | | | 720 |
| | | | | | | agg
Arg | | | | | | - | _ | | | 768 |
| | | | | _ | | gat
Asp | _ | _ | - | - | | _ | | | _ | 816 |
| _ | | _ | | _ | | cat
His | - | _ | | | Met | | - | | | 864 |
| | - | | | | | atg
Met
295 | | | | | | | _ | _ | | 912 |
| aca
Thr
305 | _ | | | | | taa
* | | | | | | | | | | 933 |

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<211> 310 <212> PRT

<213> Cenarchaeum symbiosum

<400> 44

Met Pro Ser Tyr Ala Glu Ile Ala Asn Asp Val Leu Arg Leu Met Glu Ser Val Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr Leu Ser 25 Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala Thr Asn 40 Trp Ile Thr Asp Glu Ala His Thr Ser Asn Glu Ala Leu Ile Thr Asn Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys Thr Lys 70 75 Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Val Glu Ser Thr 90 Glu Ala Ile Val Ser Tyr Ile Arg Ala Lys Phe Lys Asn Val Arg Ile 100 105 Ile Ile Pro Tyr Ala Ala Met Ser Ala Ala Ala Met Leu Ala Cys Ser 120 Ser Asn Cys Leu Val Met Gly Lys His Ser Ser Ile Gly Pro Thr Asp 135 140 Pro Gln Phe Ile Ile Pro Thr Arg Thr Gly Met His Ile Met Ser Ala 150 155 Gln Phe Leu Ile Ser Glu Phe Gln Glu Ala Gln Ser Val Ser Glu Lys 170 His Pro Gly Arg Leu Gly Ala Trp Leu Pro Leu Leu Gly Gln Tyr Pro Pro Gly Leu Ile Gln Lys Cys Ile Ser Ser Gln Lys Leu Ser Val Glu 200 Leu Val Gln Lys Trp Leu Ala Arg Tyr Met Phe Glu Asn Glu Ser Ala Ala Val Lys Lys Ser Lys Ile Ser Glu Ile Met Ser Ser Ser Lys 230 235 Lys Tyr His Ser His Gly Arg Arg Ile Ser Arg Glu Glu Cys Lys Arg 250 Ile Gly Leu Lys Val Thr Asp Leu Glu Asp Glu Glu Phe Gln Asp 265 Leu Val Leu Ser Val Phe His Ala Ala Asn Thr Met Phe Gln Tyr Thr

Thr Leu Pro Thr Pro Arg

<210> 45

<211> 1305

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(1305)

<400> 45

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275 280 285
Pro Val Asn Lys Ile Ile Met Asn His Leu Gly Asn Thr Val Val Glu

295

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| 1 | | | | 5 | | | | | 10 | | | | | 15 | | | |
|---|---|---|-------------------|---|---|---|---|---|----|---|---|---|---|----|------------|-----|---|
| | | | | | | | | | | | | | | | aac
Asn | 90 | 5 |
| | | | | | | | | | | | | | | | ggc | 144 | 1 |
| | | | gtc
Val | _ | _ | | | | | | | | | | atg
Met | 192 | } |
| | | | agc
Ser | _ | | _ | | | | _ | | | _ | | _ | 240 |) |
| - | - | | ggg
Gly | _ | | - | _ | | | | | | | _ | | 288 | ŀ |
| | _ | _ | atg
Met
100 | | | _ | | | | _ | | | _ | - | | 336 | |
| | | | aca
Thr | | | | | | | | | | | | | 384 | |
| | | | ctg
Leu | | | | | | | | | | | | | 432 | |
| | | | ggc | | | | | | | | | | | | _ | 480 | |
| | | | tat
Tyr | | | | | | | | | | | | | 528 | |
| | | | tcc
Ser
180 | | _ | | | - | | _ | | | _ | _ | _ | 576 | |
| | | | gca
Ala | | _ | _ | _ | | | | | | | _ | _ | 624 | |
| - | | | ggc
Gly | | _ | | _ | | - | | - | | _ | _ | | 672 | |
| | | _ | ttt
Phe | - | | | | | | _ | | - | | _ | | 720 | |

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| | gtg
Val | | | | | | | | Cys | | | - | _ | Ala | 768 |
|---|-------------------|--------------|---|---|---|---|-----|---|------|---|-----|-----|---|-----|------|
| | ctg
Leu | _ | | - | | | - | | _ | | _ | | | | 816 |
| | ccc
Pro | | | | | | | | | | | | | | 864 |
| | act
Thr
290 | | _ | | - | _ | | _ |
 | | | | | | 912 |
| | ttc
Phe | | _ | | | _ | _ | _ | | | | _ | | | 960 |
| | gag
Glu | | | _ | - | _ | | | | _ | | | | | 1008 |
| _ | ggg
Gly | _ | _ | _ | | _ | _ | | _ | | | | | | 1056 |
| | tcc
Ser | | | | | | | | | | | | | | 1104 |
| | ggc
Gly
370 | | | | | | | | | | | _ | - | _ | 1152 |
| | gag
Glu | | | | | | | | | | | - | _ | | 1200 |
| | ttc
Phe | | | | | | | | | | | Ala | | | 1248 |
| | gcc
Ala | | | | | | Tyr | | | | Arg | | - | _ | 1296 |
| | cta
Leu | • | | | | | | | | | | | | | 1305 |
| | | 210>
211> | | | | | | | | | | | | | |

<211> 434

<212> PRT

<213> Cenarchaeum symbiosum

<400> 46

Met Asp Leu Glu Arg Glu Tyr Arg Ala Lys Thr Gly Gly Ser Ala Arg

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10 Ile Phe Ala Arg Ser Lys Lys Tyr His Val Gly Gly Val Ser His Asn Ile Arg Phe Tyr Glu Pro Tyr Pro Phe Val Thr Arg Ser Ala Ser Gly Lys His Leu Val Asp Val Asp Gly Asn Lys Tyr Val Asp Tyr Trp Met Gly His Trp Ser Leu Ile Leu Gly His Ala Pro Ala Pro Val Arg Ser Ala Val Glu Gly Gln Leu Arg Arg Gly Trp Ile His Gly Thr Val Asn 85 90 Glu Gln Thr Met Asn Leu Ser Glu Ile Ile Arg Gly Ala Val Ser Val 105 Ala Glu Lys Thr Arg Tyr Val Thr Ser Gly Thr Glu Ala Val Met Tyr 120 Ala Ala Arg Leu Ala Arg Ala His Thr Gly Arg Lys Ile Ile Ala Lys 135 140 Ala Asp Gly Gly Trp His Gly Tyr Ala Ser Gly Leu Leu Lys Ser Val 150 Asn Trp Pro Tyr Asp Val Pro Glu Ser Gly Gly Leu Val Asp Glu Glu 165 170 His Ser Ile Ser Ile Pro Tyr Asn Asp Leu Glu Gly Ser Leu Asp Val 185 Leu Gly Arg Ala Gly Asp Asp Leu Ala Cys Val Ile Ile Glu Pro Leu 200 Leu Gly Gly Gly Cys Ile Pro Ala Asp Glu Asp Tyr Leu Arg Gly 215 Ile Gln Glu Phe Val His Ser Arg Gly Ala Leu Leu Val Leu Asp Glu 230 235 Ile Val Thr Gly Phe Arg Phe Arg Phe Gly Cys Ala Tyr Ala Ala Ala 245 250 Gly Leu Asp Pro Asp Ile Val Ala Leu Gly Lys Ile Val Gly Gly 265 Phe Pro Ile Gly Val Ile Cys Gly Lys Asp Glu Val Met Glu Ile Ser 280 Asn Thr Ile Ser His Ala Lys Ser Asp Arg Ala Tyr Ile Gly Gly 295 Thr Phe Ser Ala Asn Pro Ala Thr Met Thr Ala Gly Ala Ala Ala Leu 310 315 Gly Glu Leu Lys Lys Arg Lys Gly Thr Ile Tyr Pro Arg Ile Asn Ser 330 Met Gly Asp Asp Ala Arg Asp Lys Leu Ser Lys Ile Phe Gly Asn Arg 345 Val Ser Val Thr Gly Arg Gly Ser Leu Phe Met Thr His Phe Val Gln 360 Asp Gly Ala Gly Arg Val Ser Asn Ala Ala Asp Ala Ala Ala Cys Asp Val Glu Leu Leu His Arg Tyr His Leu Asp Met Ile Thr Arg Asp Gly 390 395 Ile Phe Phe Leu Pro Gly Lys Leu Gly Ala Ile Scr Ala Ala His Ser 410 Lys Ala Asp Leu Lys Thr Met Tyr Ser Ala Ser Glu Arg Phe Ala Glu 420 425 Gly Leu

<210> 47

<211> 807

<212> DNA

-100-

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(807)

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|------------|---|------|----|---|---|---|---|---|---|-----|---|-------------------|---|---|------------|-----|
| | | | | | | | | | | Glu | | | | | gcg
Ala | 48 |
| | | | | | | | | | | | | ata
Ile | | | | 96 |
| | | | | | | - | | | | | - | gtc
Val
45 | _ | | | 144 |
| | | _ | _ | | | _ | | | | | | gat
Asp | | | _ | 192 |
| _ | | _ | | _ | | | | _ | | _ | - | gcg
Ala | | | | 240 |
| | | _ | _ | | - | _ | _ | | | | _ | acg
Thr | _ | | | 288 |
| | | | | | | | | | | | | cgg
Arg | | | _ | 336 |
| | - | | | | _ | | _ | | - | | _ | ggc
Gly
125 | | | | 384 |
| - | | _ | _ | _ | | - | | _ | _ | | _ | gac
Asp | _ | _ | - | 432 |
| _ | | _ | | | | _ | | | | | | aag
Lys | _ | | | 480 |
| cac
His | | | | | | | | | | | | aag
Lys | | | | 528 |
| | | | | | | | | | | | | ctt
Leu | | | | 576 |
| ggc
Gly | | | | | | | | | | | | | | | | 624 |

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| cac
His | c cgc
Arg
210 | , Glu | aac
Asn | gco
n Ala | c aat
a Asr | gta
Val
215 | l Let | g tai
ı Tyı | geo
Ala | c agg | g gcg
g Ala
220 | a Arg | c ago
g Sei | c cto | c tcg
u Ser | 672 |
|-------------------|---------------------|------------------------------|-------------------|--------------|-------------------|-------------------|------------|-------------------|-------------------|---------------------|-----------------------|----------------|----------------|-------------------|-----------------------|-----|
| ggc
Gly
225 | ' Leu | ggc
Gly | agg
Arg | gag
Glu | gad
Asp
230 | Glu | tco
Sei | ata
Ile | gcg
Ala | g cad
His
235 | E Lev | g caa
ı Glr | a aag
1 Lys | g gcg
s Ala | g gcc
A Ala
240 | 720 |
| aaa
Lys | aaa
Lys | gat
Asp | tcc
Ser | Lys
245 | Thr | ata
Ile | aaa
Lys | aag
Lys | tgg
Trp
250 | Ala | cgo
Arg | gca
Ala | gaa
Glu | aag
Lys
255 | gcc
Ala | 768 |
| ttt
Phe | gac
Asp | gga
Gly | ata
Ile
260 | Arg | gac
Asp | gat
Asp | Pro | ggt
Gly
265 | tca
Ser | aaa
Lys | aga
Arg | tag | | | | 807 |
| | <
< | 210>
211>
212>
213> | 268
PRT | arch | aeum | sym | bios | um | | | | | | | | |
| Met
1 | | 400>
Leu | | Gly
5 | Lys | Ser | Asp | Pro | Ala
10 | Glu | Leu | Val | Arg | | Ala | |
| | Leu | Leu | Сув
20 | _ | Lys | Asn | Gln | Phe
25 | | Ala | Ala | Ile | - | 15
Leu | Tyr | |
| Gly | Lys | Ile
35 | | Lys | Asp | Asp | Pro | | Asn | Arg | Gly | | 30
Leu | His | Lys | |
| Lys | Gly
50 | | Ala | Gln | Asn | Arg
55 | - • | Lys | Lys | Tyr | Ser | 45
Asp | Ala | Ile | Thr | |
| Cys
65 | | Asp | Arg | Leu | Leu
70 | | Leu | Asp | Asn | Lys
75 | | Ala | Pro | Ala | _ | |
| | Asn | Lys | Ala | Ile
85 | Ala | Gln | Ala | Glu | Leu
90 | | Asp | Thr | Ala | Ser
95 | 80
Ala | |
| Leu | Glu | Asn | Tyr
100 | | Arg | Ala | Ile | Glu
105 | | Asp | Pro | Arg | Tyr | | Pro | |
| Ala | Arg | Phe
115 | Asn | Arg | Ala | Val | Leu
120 | | Asp | Arg | Leu | Gly
125 | | His | Glu | |
| Glu | Ala
130 | Leu | Pro | Asp | Leu | Asp
135 | | Ala | Ala | Glu | Leu
140 | | Arg | Arg | Lys | |
| Pro
145 | Asn | Pro | Arg | Phe | Tyr
150 | | Gly | Ile | Val | Leu
155 | | Lys | Met | Gly | Arg
160 | • |
| | Glu | Glu | | Leu
165 | Ala | Cys | Phe | Lys | Gly
170 | | Cys | Lys | Arg | His
175 | | |
| Gly | His | | | | Gln | Phe | His | Val
185 | | Ile | Glu | Leu | Thr
190 | | Leu | |
| Gly | Arg | | | Glu | Ala | Leu | Gly
200 | | Leu | Ala | Ser | Leu
205 | | Ala | Glu | |
| | Arg
210 | | Asn | Ala | Asn | Val
215 | | Tyr | Ala | Arg | Ala
220 | | Ser | Leu | Ser | |
| Gly
225 | Leu | Gly | Arg | Glu | Asp
230 | | Ser | Ile | Ala | His
235 | | Gln | Lys | Ala | | |
| | Lys | Asp | | Lys
245 | Thr | Ile | Lys | | Trp
250 | | Arg | Ala | | _ | 240
Ala | |
| Phe | Asp | | | | Asp | Asp | | | | Lys | Arg | | | 255 | | |

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gac ctg cgg gag gag ttt gcc gca aag gcg gtg gag gtg gtc tat gta 624 Asp Leu Arg Glu Glu Phe Ala Ala Lys Ala Val Glu Val Val Tyr Val 195 200 cca gtc tat gaa tcg cga ctt gtg ggg ccc aaa aaa aag gtc cgc atg 672 Pro Val Tyr Glu Ser Arg Leu Val Gly Pro Lys Lys Val Arg Met 210 atg cgg att gac gcg gca aga aaa aag atc ctc tag 708 Met Arg Ile Asp Ala Ala Arg Lys Lys Ile Leu * 230 <210> 50 <211> 235 <212> PRT <213> Cenarchaeum symbiosum <400> 50 Met Arg Gln Gly Met Thr Gly Lys Thr Arg Thr Ala Val Leu Arg Asn 5 10 Ala Met Thr Glu Glu Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr 25 Gly Ala Phe Arg Ala Leu Met Arg Ala Pro Arg Lys Glu Asp Val His Val His Ser Val Lys Leu Val His Glu Ala Leu Ile Arg Val Ser Ala 55 Arg Tyr Ser Ala Asp Phe Phe Arg Lys Ala Val His Pro Ile Lys Val 70 75 Asp Gln Asn Val Ile Glu Val Val Leu Gly Asp Gly Val Phe Pro Ile 90 85 Arg Ser Lys Ser Arg Ile His Lys Thr Leu Ser Ala Gly Leu Gly Lys 105 Asn Arg Val Asp Leu Glu Leu Glu Glu His Val Phe Ala Glu Ser Glu 120 Gly Met Met Cys Leu Asp Arg His Gly Gly Glu Thr Asp Phe Pro Tyr 135 Lys Thr Gly Pro Gly Ala Val Glu Pro Tyr Pro Arg Arg Ile Leu Asp 150 155 Ala Ser Glu Asn Val Arg Ser Pro Glu Val Glu Thr Glu Glu Ala Leu 170 Ser Lys Leu Lys Glu Lys Leu Arg Gly Pro Pro Pro Asp Gly Met Arg 180 185 Asp Leu Arg Glu Glu Phe Ala Ala Lys Ala Val Glu Val Val Tyr Val 200 Pro Val Tyr Glu Ser Arg Leu Val Gly Pro Lys Lys Val Arg Met 215 Met Arg Ile Asp Ala Ala Arg Lys Lys Ile Leu 230 <210> 51 <211> 378 <212> DNA <213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(378)

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| | - | 400> | | | | | | | | | | | | | | |
|-----|------|------|------|-----------|-----|-----------|------------------|---------|------------|-------------|-----------|-------|------------|------------------|------------|------|
| atg | agg | tcg | gag | ggc | agg | ccc | gga | tac | atc | gaa | aag | ttc | cta | aag | agg | 48 |
| Met | Arg | Ser | Glu | Gly | Arg | Pro | Gly | Tyr | | Glu | Lys | Phe | Leu | | Arg | |
| 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| | | | | | | | ~~~ | ata | ~~~ | 09 0 | ~~~ | ata | 224 | 200 | ~~ | 96 |
| | | | | | | | | | | | | | | | gca
Ala | 96 |
| ALA | мьр | Буб | 20 | 116 | nsp | ASII | AIG | 25 | 014 | 01 | O., | 741 | 30 | nr 9 | niu | |
| | | | 20 | | | | | | | | | | | | | |
| gac | gag | ata | cta | gat | gac | gca | gtc | gag | ctc | ggc | aag | atc | acc | gtg | ggc | 144 |
| Asp | Glu | Ile | Leu | Asp | Asp | Ala | Val | Glu | Leu | Gly | Lys | Ile | Thr | Val | Gly | |
| | | 35 | | | | | 40 | | | | | 45 | | | | |
| | | | | | | | | | | | | | | | | 1.00 |
| | | | | | | | | | ctc
Leu | | | | | | | 192 |
| GIU | 50 | GIII | rÀs | Arg | 261 | ASP
55 | Val | Deu | Dea | БуБ | 60 | AIG | Gru | Arg | GIU | |
| | 30 | | | | | | | | | | | | | | | |
| agc | aag | cgg | ctc | aag | tca | agg | ggc | gcc | aaa | aag | ctc | gaa | aag | ggc | ata | 240 |
| Ser | Lys | Arg | Leu | Lys | Ser | Arg | Gly | Ala | Lys | Lys | Leu | Glu | Lys | Gly | Ile | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | aag | | | | | | | 288 |
| GIY | Ala | Ala | гАз | ьуs
85 | met | Ala | Ala | GIY | Lys
90 | GIY | ASP | MIG | Leu | 95 | Int | |
| | | | | 0.5 | | | | | ,,, | | | | | ,, | | |
| ctg | gca | aag | ctc | ggc | gag | ctg | aga | aag | gcg | 999 | atc | ata | acg | gag | aag | 336 |
| | | | | | | | | | Ala | | | | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| | | | | | | | | | _ • | | | | | | | |
| | | | | | | | | | ctc
Leu | | | | tga
* | | | 378 |
| GLU | Pile | 115 | AIA | цув | цуѕ | цув | 120 | Deu | Deu | AIG | GIU | 125 | | | | |
| | | 113 | | | | | | | | | | | | | | |
| | <2 | 210> | 52 | | | | | | | | | | | | | |
| | <2 | 211> | 125 | | | | | | | | | | | | | |
| | | 212> | | | | | | | | | | | | | | |
| | <2 | 213> | Cena | ircha | eum | symb | 1051 | ım | | | | | | | | |
| | - 6 | | 52 | | | | | | | | | | | | | |
| Met | | | | Glv | Ara | Pro | Glv | Tyr | Ile | Glu | Lys | Phe | Leu | Lys | Ara | |
| 1 | 5 | | | 5 | 5 | | 2 | | 10 | | • | | | 15 | 3 | |
| Ala | Asp | Lys | Ala | Ile | qaA | Asn | Ala | Val | Glu | Gln | Gly | Val | Lys | Arg | Ala | |
| | | | 20 | | | | | 25 | | | | | 30 | | | |
| Asp | Glu | | Leu | qaA | qaA | Ala | | Glu | Leu | Gly | Lys | | Thr | Val | Gly | |
| | _ • | 35 | _ | _ | _ | _ | 40 | • | . | . | 61 | 45 | a 1 | _ | ~3 | |
| GIU | | Gin | гàг | Arg | ser | _ | vaı | Leu | Leu | гÀг | GIN | AIa | GIU. | Arg | GIU | |
| Ser | 50 | Ara | Lan | Lare | Sar | 55
Ara | Glv | Δla | Lys | Lvs | | Glu | Lve | Glv | Tle | |
| 65 | Lys | AI 9 | пец | Буз | 70 | Ar 9 | G ₂ y | <i></i> | Dyo | 75 | Deu | O L u | 275 | O ₁ y | 80 | |
| | Ala | Ala | Lvs | Lys | - | Ala | Ala | Gly | Lys | _ | Asp | Ala | Leu | Glu | | |
| | | | | 85 | | | | • | 90 | • | • | | | 95 | | |
| Leu | Ala | Lys | Leu | Gly | Glu | Leu | Arg | Lys | Ala | Gly | Ile | Ile | Thr | Glu | Lys | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| Glu | Phe | _ | Ala | Lys | Lys | Lys | | Leu | Leu | Ala | Glu | | | | | |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| | | | | | | | | | | | | | | | | |

<210> 53 <211> 606 -105-

| | < | 212> | DNA | | | | | | | | | | | | | |
|------|------|------|-----|------------|--------------|-----|-----------|-----|------------|------|-------------|------------|-------------|------------|-----|-----|
| | < | 213> | Cen | arch | aeum | sym | bios | um | | | | | | | | |
| | < | 220> | | | | | | | | | | | | | | |
| | | | CDS | | | | | | | | | | | | | |
| | < | 222> | (1) | (| 606) | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| ato | | 400> | | aaa | acc | tcc | cca | aaa | gga | tat | acc | tac | aco | cca | tac | 48 |
| | | | | | | | | | | | | | | | Tyr | 40 |
| 1 | | - | | 5 | | | | - | 10 | | | - | | 15 | _ | |
| | | | | | | | | | | | | | | | | |
| _ | | - | | - | _ | | | | _ | | | rgg | | _ | tcg | 96 |
| 1111 | 1115 | rop | 20 | nia | 361 | 116 | GIU | 25 | - | GIU | 51 u | 110 | 30 | | 561 | |
| | | | | | | | | | | | | | | | | |
| | | - | | | _ | | | | | | | ttc | - | | | 144 |
| Arg | ASN | 735 | GIY | GIU | мет | Tyr | Pne
40 | vai | inr | Ala | Thr | Phe
45 | ser | Ser | гàг | |
| | | 33 | | | | | -20 | | | | | 13 | | | | |
| | | | | | | | | | | | | ctg | - | _ | | 192 |
| Ser | | Pro | Tyr | Phe | Glu | | Gln | Ala | Ser | His | _ | Leu | Leu | Ala | Arg | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| ttc | aaa | aac | ggc | ccc | aaa | atg | ata | aag | gcg | gtg | gag | ggc | cgc | 999 | ggc | 240 |
| | Lys | Asn | Gly | Pro | - | Met | Ile | Lys | Ala | | Glu | Gly | Arg | Gly | • | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| ggc | cct | tec | tat | tta | ttc | agc | atg | gac | gag | gag | ata | ttc | gaa | agg | gaa | 288 |
| | | | | | | | | | | | | Phe | | | _ | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| tcc | ccc | aga | ato | age | tat | gta | tcc | atq | tac | tat | cta | gaa | tac | ασa | gat | 336 |
| | | | | | | | | | | | | Glu | | | | |
| | | | 100 | | | | | 105 | | | | | 110 | | | |
| t.cc | gag | gag | gac | ata | cac | gag | at.a | aca | t.ca | σt.a | at.a | gca | aga | αασ | αaα | 384 |
| | | | | | | | | | | | | Ala | _ | _ | | 304 |
| | | 115 | | | | | 120 | | | | | 125 | | | | |
| 226 | 2+2 | aac | 200 | 909 | ~ ~ = | 2+2 | aaa | cac | ato | as t | at a | tgc | + 00 | 200 | 244 | 432 |
| | | | | | | | | | | | | Cys | | | | 432 |
| - | 130 | - | | | • | 135 | - | • | | - | 140 | • | | - 3 | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | gtg
Val | | | | 480 |
| 145 | | -,- | | | 150 | | -,- | 001 | 01, | 155 | | ••• | V 41 | Deu | 160 | |
| | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | tac | _ | _ | _ | 528 |
| vaı | ser | ser | GIU | ьуs
165 | ser | нів | GIN | ser | val
170 | Asn | гуѕ | Tyr | Cys | GIu
175 | Lys | |
| | | | | - 43 | | | | | _,, | | | | | 1/5 | | |
| | | | | | | | | | | _ | _ | acc | | | _ | 576 |
| Thr | Arg | Arg | | Val | Ile | Arg | Lys | _ | Ile | Thr | Met | Thr | | Leu | Val | |
| | | | 180 | | | | | 185 | | | | | 190 | | | |
| agc | ctg | tcg | ata | ctg | gag | agg | ctc | aaa | taa | | | | | | | 606 |
| | | | Ile | | | | | | * | | | | | | | |
| | | | | | | | | | | | | | | | | |

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195 200 <210> 54 <211> 201 <212> PRT <213> Cenarchaeum symbiosum Met Ser Lys Thr Glu Ala Ser Pro Gly Gly Tyr Ala Cys Thr Pro Tyr Thr His Asp His Ala Ser Ile Glu Leu Lys Glu Glu Trp Ser Ser Ser 25 Arg Asn Val Gly Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Lys 40 Ser Lys Pro Tyr Phe Glu Gln Gln Ala Ser His Tyr Leu Leu Ala Arg Phe Lys Asn Gly Pro Lys Met Ile Lys Ala Val Glu Gly Arg Gly Gly 70 75 Gly Pro Ser Tyr Leu Phe Ser Met Asp Glu Glu Ile Phe Glu Arg Glu Ser Pro Gly Met Ser Tyr Val Ser Met Tyr Tyr Leu Glu Tyr Gly Asp 105 Ser Glu Glu Asp Ile Arg Glu Val Ala Ser Val Val Ala Arg Lys Glu 120 Lys Ile Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Ile 135 140 Pro Pro Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Val Val Leu Glu 150 155 Val Ser Ser Glu Lys Ser His Gln Ser Val Asn Lys Tyr Cys Glu Lys 170 Thr Arg Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val 185 Ser Leu Ser Ile Leu Glu Arg Leu Lys 195 200 <210> 55 <211> 822 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(822) <400> 55 ttg aaa agt acg ttg gtt cgg cgc tac aag ccc aag ata aag cag acc 48 Met Lys Ser Thr Leu Val Arg Arg Tyr Lys Pro Lys Ile Lys Gln Thr 5 ctc cgc gag gtg ccc ctc aaa aat gtg cat gtg tgg aag gag gcg cag 96 Leu Arg Glu Val Pro Leu Lys Asn Val His Val Trp Lys Glu Ala Gln

Ala Arg Arg Leu Asp Arg Ser Arg Val Arg Asp Ile Ala Lys Ser Ile 35 40 45

144

gca agg agg ctg gac agg tcc cgg gtg cgg gat atc gca aag tcg atc

aga tca gag ggg ctg cag aac ccg ccc gtc ata cag agg ggc ggc agg 192

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| Arg | Ser
50 | | Gly | Leu | Gln | Asn
55 | Pro | Val | Ile | Gln
60 | _ | Gly | Gly | Arg | | |
|-------------------|-----------|-----|-----|-----|-----|-----------|-------------------|-----|-----|-----------|-----|-----|-----|------------------|----|-----|
| | | | | | | Ser | | | | Leu | | | | aag
Lys
80 | : | 240 |
| | | | | | | | | | | | | | | aca
Thr | 2 | 288 |
| | | | _ | | | | gcc
Ala
105 | - | | | _ | | | ctg
Leu | 3 | 336 |
| | | | | | | | gag
Glu | | | | | | | | 3 | 884 |
| | | | | | | | gag
Glu | | | | | | | | 4 | 32 |
| | | | | | | | cac
His | | | | | | | | 4 | 80 |
| | | | | | _ | | acc
Thr | | | | - | | | | 5 | 28 |
| | | | | | | | ata
Ile
185 | | | | | | | | 5 | 76 |
| | | | | | | | ccg
Pro | | | | | | | | 6: | 24 |
| ttg
Leu | | | | | | | ggc
Gly | | | | | | | | 6 | 72 |
| atg
Met
225 | | | | | | | | | | | | | | | 7: | 20 |
| aac
Asn | | | | | | | | | | | | | | | 7(| 68 |
| gag
Glu | | Arg | | | | | | | | | Leu | | | | 81 | 16 |
| cga
Arg | tga
* | | | | | | | | | | | | | | 82 | 22 |
| | | | | | | | | | | | | | | | | |

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<210> 56 <211> 273 <212> PRT

<213> Cenarchaeum symbiosum

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Arg

<210> 57 <211> 669 <212> DNA <213> Cenarchaeum symbiosum

<220> <221> CDS <222> (1)...(669)

<400> 57

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Met Ala Arg Ser Pro Val Leu Ile Ile Asn Cys Lys Asn Tyr Lys Glu
1 5 10 15

265

gcg gcc ggc ggc aga att gac agc cta gcg gcg gca gcc gcc ggg gcg 96 Ala Ala Gly Gly Arg Ile Asp Ser Leu Ala Ala Ala Ala Ala Gly Ala

| | | | 20 | | | | | 25 | i | | | | 30 |) | | | |
|------------|----------|--------------------------|------------|-----------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|---|-----|
| _ | _ | | Tyr | | _ | | | Ala | | _ | _ | _ | Gln | | ctg
Leu | | 144 |
| | | Ala | _ | | | | | | | | _ | Ala | _ | | ata
Ile | | 192 |
| | | | | | | | | | | | | gtg
Val | _ | | _ | | 240 |
| | | | | | | | | | | | | cac
His | _ | _ | | | 288 |
| | | | | | | | | | | | | agg
Arg | | | | | 336 |
| | | | | | | | | | | | | gcc
Ala
125 | | | | | 384 |
| | | | | | | | | | | | | gag
Glu | | | | • | 432 |
| | | | | | | | | | | | | ccc
Pro | | | | | 480 |
| | | | | | | | | | | | | aca
Thr | | | | | 528 |
| | | | | | | | | | | | | aag
Lys | | | | | 576 |
| ctc
Leu | ggc | tcc
Ser
195 | aag
Lys | gj
gaa | atc
Ile | ctc
Leu | gtg
Val
200 | gca
Ala | agc
Ser | ggg
ggg | gtg
Val | gta
Val
205 | aaa
Lys | tca
Ser | tca
Ser | • | 524 |
| | | | | | Ile | | | | | | | atg
Met | | tga
* | | € | 69 |
| | <2
<2 | 10>
11>
12>
13> | 222
PRT | rcha | eum | symb | iosu | ım | | | | | | ٠ | | | |
| | <4 | 00> | 58 | | | - | | | . , | | | | | | | | |

Met Ala Arg Ser Pro Val Leu Ile Ile Asn Cys Lys Asn Tyr Lys Glu

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Ala Ala Gly Gly Arg Ile Asp Ser Leu Ala Ala Ala Ala Gly Ala Ala Ala Lys Tyr Gly Val Arg Ile Ala Leu Ala Pro Pro Gln His Leu 40 Leu Gly Ala Val Lys Gly Glu Asp Leu Thr Val Leu Ala Gln His Ile 55 Asp Asp Lys Gly Val Gly Ser Thr Thr Gly Tyr Val Val Pro Glu Leu 70 75 Leu Gly Glu Ser Gly Val Ser Gly Ala Leu Ile Asn His Ser Glu His 85 90 Arg Val Ser Ala Asp Gln Val Ala Ser Leu Val Pro Arg Leu Arg Gly Leu Asp Met Ile Ser Val Val Cys Val Lys Asp Ser Ala Glu Ala Ala 120 Asn Leu Ser Arg His Arg Pro Asp Tyr Ile Ala Ile Glu Pro Pro Glu 135 Leu Ile Gly Ser Gly Arg Ser Val Ser Ser Glu Arg Pro Glu Leu Ile 150 155 Gly Glu Ala Ala Glu Ala Ile Arg Gly Ala Asp Gly Thr Lys Leu Leu 170 165 Cys Gly Ala Gly Ile Thr Ser Gly Ala Asp Val Arg Lys Ala Leu Glu 185 Leu Gly Ser Lys Gly Ile Leu Val Ala Ser Gly Val Val Lys Ser Ser 200 205 Asp Pro Ala Ala Ile Ala Glu Leu Ala Gln Ala Met Ser 215 <210> 59 <211> 549 <212> DNA <213> Cenarchaeum symbiosum · <220> <221> CDS <222> (1)...(548) <400> 59 atg ctg gat ccc cgg acg cgc ccc cgg gtc gtc aat gtc gtc agc aca Met Leu Asp Pro Arg Thr Arg Pro Arg Val Val Asn Val Val Ser Thr tca gac ctt gta caa agg gtg agc gca aaa aag atg gcc gcc atg ccg Ser Asp Leu Val Gln Arg Val Ser Ala Lys Lys Met Ala Ala Met Pro 20 tge tge atg tat gat gag gee gta tae gge gge agg tge gge tae ata 144 Cys Cys Met Tyr Asp Glu Ala Val Tyr Gly Gly Arg Cys Gly Tyr Ile aag acg ccc ggc atg cag ggg agg gtg act gta ttc att tct ggc aag 192 Lys Thr Pro Gly Met Gln Gly Arg Val Thr Val Phe Ile Ser Gly Lys 55 atg ata tee gte gge gee aga tee gtg agg gee teg ttt ggg cag etg 240 Met Ile Ser Val Gly Ala Arg Ser Val Arg Ala Ser Phe Gly Gln Leu 70 75 cac gag gcg cgg ctc cac ctg gtg cgc aac ggg gct gcc ggc gac tgc 288

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| | | | | | | | | | -111 | | | | | | | |
|---|--|---|--|--|--|--|--|--|--|--|--|--|---|--|--|-----|
| His | Glu | Ala | Arg | Leu
85 | His | Leu | Val | Arg | Asn
90 | Gly | Ala | Ala | Gly | Asp
95 | Cys | |
| aag
Lys | ata
Ile | agg
Arg | ccc
Pro
100 | gtc
Val | gtg
Val | cgc
Arg | aat
Asn | att
Ile
105 | gta
Val | gcc
Ala | acg
Thr | gtg
Val | gat
Asp
110 | gcc
Ala | ggt
Gly | 336 |
| agg
Arg | aat
Asn | gtt
Val
115 | ccc
Pro | ata
Ile | gac
Asp | agg
Arg | ata
Ile
120 | tcg
Ser | tcg
Ser | cgc
Arg | atg
Met | cct
Pro
125 | ggc
Gly | gct
Ala | gta
Val | 384 |
| tat
Tyr | gat
Asp
130 | ccc
Pro | gjå
aaa | tcg
Ser | ttt
Phe | ccc
Pro
135 | ggg
Gly | atg
Met | ata
Ile | ctc
Leu | aag
Lys
140 | gj
ggg | ctg
Leu | gac
Asp | agc
Ser | 432 |
| tgc
Cys
145 | agc
Ser | ttt
Phe | cta
Leu | gtc
Val | ttt
Phe
150 | gcg
Ala | tcg
Ser | gga
Gly | aag
Lys | atg
Met
155 | gtg
Val | ata
Ile | gcg
Ala | ggc
Gly | gcc
Ala
160 | 480 |
| aag
Lys | tcg
Ser | ccg
Pro | gat
Asp | gag
Glu
165 | ctg
Leu | cgc
Arg | agg
Arg | tcg
Ser | tcg
Ser
170 | ttt
Phe | gac
Asp | ctg
Leu | ctg
Leu | acg
Thr
175 | cgc
Arg | 528 |
| | | | | gjå
aaa | | ta ç | 3 | | | | | | | | | 549 |
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400> | PRT
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Leu | 212>
213>
400>
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Cena
60
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Val | Arg
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15
Met | | |
| 1
Ser
Cys | Leu
Asp | 212>
213>
400>
Asp
Leu
Met
35 | PRT
Cens
60
Pro
Val
20
Tyr | Arg
5
Gln
Asp | Thr
Arg
Glu | Arg
Val
Ala | Pro
Ser
Val
40 | Arg
Ala
25
Tyr | 10
Lys
Gly | Lys
Gly | Met
Arg | Ala
Cys
45 | Ala
30
Gly | 15
Met
Tyr | Pro
Ile | |
| 1
Ser
Cys
Lys | Leu
Asp
Cys | 212>
213>
400>
Asp
Leu
Met
35
Pro | PRT
Cens
60
Pro
Val
20
Tyr | Arg
5
Gln
Asp
Met | Thr
Arg
Glu
Gln | Arg
Val
Ala
Gly
55 | Pro
Ser
Val
40
Arg | Arg
Ala
25
Tyr
Val | 10
Lys
Gly
Thr | Lys
Gly
Val | Met
Arg
Phe
60 | Ala
Cys
45
Ile | Ala
30
Gly
Ser | 15
Met
Tyr
Gly | Pro
Ile
Lys | |
| 1
Ser
Cys
Lys
Met | Leu
Asp
Cys
Thr | 212>
213>
400>
Asp
Leu
Met
35
Pro | PRT
Cens
60
Pro
Val
20
Tyr
Gly
Val | Arg
5
Gln
Asp
Met | Thr Arg Glu Gln Ala 70 | Arg
Val
Ala
Gly
55
Arg | Pro
Ser
Val
40
Arg | Arg Ala 25 Tyr Val | 10
Lys
Gly
Thr
Arg | Lys
Gly
Val
Ala
75 | Met
Arg
Phe
60
Ser | Ala
Cys
45
Ile
Phe | Ala
30
Gly
Ser | 15
Met
Tyr
Gly
Gln | Pro Ile Lys Leu 80 | |
| Ser
Cys
Lys
Met
65 | Leu Asp Cys Thr 50 Ile | 212>
213>
400>
Asp
Leu
Met
35
Pro
Ser | PRT
Cend
60
Pro
Val
20
Tyr
Gly
Val
Arg | Arg
5
Gln
Asp
Met
Gly
Leu
85 | Thr Arg Glu Gln Ala 70 His | Arg
Val
Ala
Gly
55
Arg
Leu | Pro
Ser
Val
40
Arg
Ser
Val | Arg Ala 25 Tyr Val Val Arg | 10
Lys
Gly
Thr
Arg
Asn
90 | Lys
Gly
Val
Ala
75
Gly | Met Arg Phe 60 Ser Ala | Ala
Cys
45
Ile
Phe
Ala | Ala
30
Gly
Ser
Gly | 15
Met
Tyr
Gly
Gln
Asp
95 | Pro Ile Lys Leu 80 Cys | |
| 1
Ser
Cys
Lys
Met
65
His | Leu Asp Cys Thr 50 Ile Glu | 212>
213>
400>
Asp
Leu
Met
35
Pro
Ser
Ala | PRT Cend 60 Pro Val 20 Tyr Gly Val Arg | Arg
5
Gln
Asp
Met
Gly
Leu
85
Val | Thr Arg Glu Gln Ala 70 His | Arg
Val
Ala
Gly
55
Arg
Leu | Pro
Ser
Val
40
Arg
Ser
Val | Arg Ala 25 Tyr Val Val Arg Ile 105 | 10
Lys
Gly
Thr
Arg
Asn
90
Val | Lys Gly Val Ala 75 Gly Ala | Met Arg Phe 60 Ser Ala Thr | Ala
Cys
45
Ile
Phe
Ala
Val | Ala 30 Gly Ser Gly Gly Asp 110 | 15
Met
Tyr
Gly
Gln
Asp
95
Ala | Pro Ile Lys Leu 80 Cys | |
| Ser
Cys
Lys
Met
65
His
Lys | Leu Asp Cys Thr 50 Ile Glu Ile | 212>
213>
400>
Asp
Leu
Met
35
Pro
Ser
Ala
Arg | PRT
Cens
60
Pro
Val
20
Tyr
Gly
Val
Arg
Pro
100
Pro | Arg 5 Gln Asp Met Gly Leu 85 Val | Thr Arg Glu Gln Ala 70 His Val | Arg Val Ala Gly 55 Arg Leu Arg | Pro
Ser
Val
40
Arg
Ser
Val
Asn
Ile
120 | Arg Ala 25 Tyr Val Val Arg Ile 105 Ser | IO
Lys
Gly
Thr
Arg
Asn
90
Val | Lys Gly Val Ala 75 Gly Ala Arg | Met Arg Phe 60 Ser Ala Thr | Ala Cys 45 Ile Phe Ala Val Pro 125 | Ala
30
Gly
Ser
Gly
Gly
Asp
110
Gly | 15
Met
Tyr
Gly
Gln
Asp
95
Ala
Ala | Pro Ile Lys Leu 80 Cys Gly Val | |
| 1
Ser
Cys
Lys
Met
65
His
Lys
Arg | Leu Asp Cys Thr 50 Ile Glu Ile Asn Asp | 212> 213> 400> Asp Leu Met 35 Pro Ser Ala Arg | PRT Cens 60 Pro Val 20 Tyr Gly Val Arg Pro 100 Pro | Arg 5 Gln Asp Met Gly Leu 85 Val Ile | Thr Arg Glu Gln Ala 70 His Val Asp | Arg Val Ala Gly 55 Arg Leu Arg Arg Pro | Pro
Ser
Val
40
Arg
Ser
Val
Asn
Ile
120
Gly | Arg Ala 25 Tyr Val Val Arg Ile 105 Ser | IO
Lys
Gly
Thr
Arg
Asn
90
Val
Ser
Ile | Lys Gly Val Ala 75 Gly Ala Arg Leu | Met Arg Phe 60 Ser Ala Thr Met Lys 140 | Ala Cys 45 Ile Phe Ala Val Pro 125 Gly | Ala
30
Gly
Ser
Gly
Gly
Asp
110
Gly
Leu | 15
Met
Tyr
Gly
Gln
Asp
95
Ala
Ala
Asp | Pro Ile Lys Leu 80 Cys Gly Val Ser | |
| 1
Ser
Cys
Lys
Met
65
His
Lys
Arg | Leu Asp Cys Thr 50 Ile Glu Ile Asn Asp | 212> 213> 400> Asp Leu Met 35 Pro Ser Ala Arg | PRT Cens 60 Pro Val 20 Tyr Gly Val Arg Pro 100 Pro | Arg 5 Gln Asp Met Gly Leu 85 Val Ile | Thr Arg Glu Gln Ala 70 His Val Asp Phe | Arg Val Ala Gly 55 Arg Leu Arg Arg Pro | Pro
Ser
Val
40
Arg
Ser
Val
Asn
Ile
120
Gly | Arg Ala 25 Tyr Val Val Arg Ile 105 Ser | IO
Lys
Gly
Thr
Arg
Asn
90
Val
Ser
Ile | Lys Gly Val Ala 75 Gly Ala Arg Leu Met | Met Arg Phe 60 Ser Ala Thr Met Lys 140 Val | Ala Cys 45 Ile Phe Ala Val Pro 125 Gly | Ala
30
Gly
Ser
Gly
Gly
Asp
110
Gly
Leu | 15
Met
Tyr
Gly
Gln
Asp
95
Ala
Ala | Pro Ile Lys Leu 80 Cys Gly Val Ser Ala | |
| 1
Ser
Cys
Lys
Met
65
His
Lys
Arg
Tyr | Leu Asp Cys Thr 50 Ile Glu Ile Asn Asp | 212> 213> 400> Asp Leu Met 35 Pro Ser Ala Arg Val 115 Pro | PRT Cens 60 Pro Val 20 Tyr Gly Val Arg Pro 100 Pro | Arg 5 Gln Asp Met Gly Leu 85 Val Ile Ser | Thr Arg Glu Gln Ala 70 His Val Asp Phe 150 Leu | Arg Val Ala Gly 55 Arg Leu Arg Pro 135 Ala | Pro Ser Val Arg Ser Val Asn Ile 120 Gly Ser | Arg Ala 25 Tyr Val Val Arg Ile 105 Ser Met Gly | IO
Lys
Gly
Thr
Arg
Asn
90
Val
Ser
Ile | Lys Gly Val Ala 75 Gly Ala Arg Leu Met 155 Phe | Met Arg Phe 60 Ser Ala Thr Met Lys 140 Val | Ala Cys 45 Ile Phe Ala Val Pro 125 Gly Ile | Ala 30 Gly Ser Gly Gly Asp 110 Gly Leu Ala | Tyr Gly Gln Asp 95 Ala Ala Asp Gly | Pro Ile Lys Leu 80 Cys Gly Val Ser | |

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| | | | _ | | _ | | Asp | | | | _ | Ser | | gag
Glu | 624 |
|-----------------------|---|---|---|---|---|---|-----|---|---|---|---|-----|---|-------------------|------|
| | | • | | | | | | | | | | | | gtg
Val | 672 |
|
Phe | - | _ | | _ | | | - | _ | _ | | _ | _ | _ | agc
Ser
240 | 720 |
| gcg
Ala | | | | _ | | | | | | | _ | | | | 768 |
| tac
Tyr | _ | | _ | _ | | | _ | _ | | _ | _ | | | _ | 816 |
| ata
Ile | | _ | | _ | | _ | | | | | | _ | _ | | 864 |
| atg
Met
290 | | | | | | | | | | | | | | | 912 |
| gac
Asp | | | | | | | | | | | | | | | 960 |
| gtc
Val | | _ | - | _ | | | | | _ | | | _ | | _ | 1008 |
| tat
Tyr | - | | _ | _ | _ | | | _ | | | _ | | _ | | 1056 |
| aag
Lys | | _ | | | - | | _ | | | | | | | | 1104 |
|
gat
Asp
370 | | | | | _ | | _ | | | _ | | | _ | | 1152 |
| ctg
Leu | | | | | | | | | | | | | | | 1200 |
| ctg
Leu | | | | | | | Ala | | | | | | | | 1248 |
| cgc
Arg | | | | | | | | | | | | | | | 1296 |

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| | | 420 | | | | 425 | | | | | 430 | | | |
|---|-------|-----|---|-------------------|---|-----|---|---|---|-----|-----|---|------------|------|
| |
- | Arg | | | - | | _ | | _ | | _ | _ | aag
Lys | 1344 |
| | | | | agc
Ser | | | | | | Asp | | _ | | 1392 |
| _ |
 | | _ | gtc
Val
470 | | _ | | | | | | - | _ | 1440 |
| | | | | gca
Ala | | | | | | | _ | | _ | 1488 |
| | | | | acc
Thr | | | | | | | | | | 1536 |
| | | | | acc
Thr | | | | | | | | | | 1584 |
| | | | | ata
Ile | | | | | | | | | | 1632 |
| | | | | aag
Lys
550 | | | | | | | | | | 1680 |
| | | | | agc
Ser | | | | | | | | | | 1728 |
| |
 | _ | | gcc
Ala | | | _ | _ | | | _ | | _ | 1776 |
| | | | | gcg
Ala | | | | | | | | | | 1824 |
| | | | | atg
Met | | | | | | | | | | 1872 |
| | | | | aat
Asn
630 | | | | | | | | | | 1920 |
| | | Lys | | gag
Glu | | Val | | | | | | | | 1968 |

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| | | | _ | Val | | | | | Lys | | | | | Gly | gtg
Val | 2016 | |
|------------|-----|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-----|-----|------------|------------|------------|------|--|
| | _ | | | _ | _ | _ | _ | _ | | _ | _ | | Lys | _ | tcg
Ser | 2064 | |
| | _ | | _ | | | aag
Lys
695 | | _ | | | _ | _ | | - | ata
Ile | 2112 | |
| | _ | _ | _ | - | | gag
Glu | | | | | _ | | _ | | _ | 2160 | |
| | | | | | | gca
Ala | | | | | | | | | | 2208 | |
| | | | | | | gcg
Ala | | | | | | _ | _ | | | 2256 | |
| | | | | | | gtc
Val | | | | | | | | | _ | 2304 | |
| | | | | | | gtc
Val
775 | | | | | | | _ | | _ | 2352 | |
| Lys
785 | Val | Met | Asn | Lys | Thr
790 | • | Val | Lys | Pro | Val
795 | Glu | Met | Ala | Gln | Ala
800 | 2400 | |
| gga
Gly | Glu | Val | Asp | Thr
805 | Ser | Lys | Tyr | Leu | Glu
810 | Phe | Met | Glu | Ser | Thr
815 | Leu | 2448 | |
| gac
Asp | Gln | Leu | Thr
820 | Ser | Ser | Met | Gly | Leu
825 | Asp | Phe | Asp | Glu | Met
830 | | | 2496 | |
| aag
Lys | Pro | Lув
835 | Gln | | | _ | | | | | | | tga
* | | | 2538 | |
| | | 10> | | | | | | | | | | | | | | | |
| | | 11> | | | | | | | | | | | | | | | |
| | | 12> | | | | | . : | | | | | | | | | | |
| | <2 | 13> | cena | rcna | eum | symb | ıosu | .rn | | | | | | | | | |

<400> 62

Met Thr Ala Gln Asp Glu Glu Ile Pro Pro Ser Leu Leu Val Ser Ala 1 5 5 1 10 15 15 Thr Tyr Asp Gly Gln Ala Arg Ala Val Val Leu Lys Phe Tyr Glu Ser 20 25 25 30 -116-

Glu Ser Gln Lys Ile Ile His Trp Thr Asp Asn Thr Gly His Lys Pro 40 Tyr Cys Tyr Thr Arg Leu Pro Pro Ser Glu Leu Gly Phe Leu Gly Gly Arg Glu Asp Val Leu Gly Ile Glu Gln Val Met Arg His Asp Leu Ile Ala Asp Lys Glu Val Pro Val Ser Lys Ile Thr Val Ser Asp Pro Leu 90 85 Ala Ile Gly Gly Thr His Ser Glu Lys Ser Ile Arg Asn Val Ile Asp 105 Thr Trp Glu Ser Asp Ile Lys Tyr Tyr Glu Asn Tyr Leu Tyr Asp Ala 120 Gly Leu Val Val Gly Arg Tyr Tyr Ser Val Ser Gly Gly Glu Val Ile 140 135 Pro His Asp Met Pro Ile Ser Asp Glu Val Lys Leu Ala Leu Lys Ser 150 155 Leu Leu Trp Asp Lys Leu Ile Asp Glu Gly Met Ala Asp Arg Lys Glu 170 Phe Arg Glu Phe Ile Ala Gly Trp Ala Asp Leu Leu Asn Gln Pro Ile 185 Pro Arg Ile Arg Arg Leu Ser Phe Asp Ile Glu Val Asp Ser Glu Glu 200 Gly Arg Ile Pro Asp Ala Lys Ile Ser Asp Arg Arg Val Thr Ala Val 215 220 Gly Phe Ala Ala Thr Asp Gly Leu Arg Lys Val Leu Val Leu Lys Ser 230 235 Gly Ala Asp Glu Gly Ala Asn Asp Val Thr Pro Gly Val Glu Val Val 245 250 Phe Tyr Asp Glu Asp Lys Glu Ala Asp Met Ile Arg Asp Ala Leu Ala 260 265 Ile Ile Gly Ser Tyr Pro Phe Val Leu Thr Tyr Asn Gly Asp Asp Phe 280 Asp Met Pro Tyr Met Tyr Asn Arg Ala Arg Arg Leu Gly Val Ala Asp 295 300 Ser Asp Ile Pro Leu Tyr Met Met Arg Asp Ser Ala Thr Leu Arg His 310 315 Gly Val His Leu Asp Leu Tyr Arg Thr Phe Ser Asn Arg Ser Phe Gln 325 330 Leu Tyr Ala Phe Ala Ala Lys Tyr Thr Asp Tyr Ser Leu Asn Ser Val 345 Ser Lys Ala Met Leu Gly Glu Gly Lys Val Asp Tyr Gly Val Ser Leu 360 365 Gly Asp Leu Thr Leu Tyr Gln Thr Ala Asn Tyr Cys Tyr His Asp Ala 375 380 Arg Leu Thr Leu Glu Leu Ser Thr Phe Gly Asn Glu Ile Leu Met Asp 395 390 Leu Leu Val Val Thr Ser Arg Ile Ala Arg Met Pro Ile Asp Asp Met 410 Ser Arg Met Gly Val Ser Gln Trp Ile Arg Ser Leu Leu Tyr Tyr Glu 425 His Arg Gln Arg Asn Ala Leu Ile Pro Arg Arg Asp Glu Leu Glu Lys 440 Arg Ser Gln Gln Val Ser Asn Asp Ala Val Ile Lys Asp Lys Lys Phe 455 460 Arg Gly Gly Leu Val Val Glu Pro Glu Glu Gly Ile His Phe Asp Val 470 475 Thr Val Met Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Lys Val Arg 490 485

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```
Asn Leu Ser Tyr Glu Thr Val Arg Cys Val His Pro Glu Cys Arg Lys
                                505
Asn Thr Ile Pro Asp Thr Asn His Trp Val Cys Thr Lys Asn Asn Gly
                           520
Leu Thr Ser Met Ile Ile Gly Ser Leu Arg Asp Leu Arg Val Asn Tyr
                        535
Tyr Lys Ser Leu Ser Lys Ser Gln Ser Ile Thr Glu Glu Gln Arg Gln
                    550
                                       555
Gln Tyr Thr Val Ile Ser Gln Ala Leu Lys Val Val Leu Asn Ala Ser
               565
                                   570
Tyr Gly Val Met Gly Ala Glu Ile Phe Pro Leu Tyr Phe Leu Pro Ala
                               585
Ala Glu Ala Thr Thr Ala Val Gly Arg Tyr Ile Ile Met Gln Thr Ile
                         600
Ser His Cys Glu Gln Met Gly Val Lys Val Leu Tyr Gly Asp Thr Asp
                       615
                                           620
Ser Leu Phe Ile Lys Asn Pro Glu Glu Arg Gln Ile His Asp Ile Val
                                       635
Glu His Ala Lys Lys Glu His Gly Val Glu Leu Glu Val Asp Lys Glu
                645
                                   650
Tyr Arg Tyr Val Val Leu Ser Asn Arg Lys Lys Asn Tyr Phe Gly Val
                               665
Thr Lys Ser Gly Lys Val Asp Val Lys Gly Leu Thr Gly Lys Lys Ser
                          680
His Thr Pro Pro Phe Ile Lys Glu Leu Phe Tyr Ser Leu Leu Asp Ile
                       695
Leu Ser Ala Val Gln Thr Glu Asp Glu Phe Glu Ser Ala Lys Leu Lys
                   710
                                       715
Ile Ser Lys Ala Ile Ala Ala Ser Gly Lys Arg Leu Glu Glu Arg Gly
               725
                                   730
Val Pro Leu Ala Asp Leu Ala Phe Asn Val Met Ile Ser Lys Ala Pro
           740
                               745
Ser Glu Tyr Val Lys Thr Val Pro Gln His Ile Arg Ala Ala Arg Leu
                           760
Leu Glu Asn Ala Arg Glu Val Lys Lys Gly Asp Ile Ile Ser Tyr Val
                       775
Lys Val Met Asn Lys Thr Gly Val Lys Pro Val Glu Met Ala Gln Ala
                   790
                                       795 ·
Gly Glu Val Asp Thr Ser Lys Tyr Leu Glu Phe Met Glu Ser Thr Leu
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Asp Gln Leu Thr Ser Ser Met Gly Leu Asp Phe Asp Glu Met Leu Gly
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Lys Pro Lys Gln Thr Gly Met Glu Gln Phe Phe Lys
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Met Pro Val Met Cys Ala Val Ser Thr Arg Gly Pro Asp Ala Ala Cys

1 10 15

48

<400> 63

WO 00/18909 PCT/US99/22752

| | | | | Ser | | | | | Tyr | | | | | Arg | gcg
Ala | 96 |
|-----|-------------------|-----|-----|-----|---|-----|---|---|-----|---|-----|-------------------|-----|-----|------------------|-----|
| | | | | | | | | | | | | | | | gaa
Glu | 144 |
| | | | _ | _ | | | | | | | | tcc
Ser | | _ | _ | 192 |
| _ | _ | _ | | | _ | _ | | _ | | _ | | agg
Arg | _ | _ | gcc
Ala
80 | 240 |
| | | | | | _ | | | | _ | _ | | tgc
Cys | | | | 288 |
| | _ | - | | _ | | | _ | _ | | | _ | atc
Ile | _ | | | 336 |
| | | _ | _ | | _ | _ | _ | | | _ | | gcc
Ala
125 | | - | | 384 |
| | | | | | | | | | | | | ggc
Gly | | - | | 432 |
| | | | | | | | | | | | | aag
Lys | | | | 480 |
| | | | | | | | | | | | | tat
Tyr | | | | 528 |
| | | | | | | | | | | | | acc
Thr | | | | 576 |
| _ | Glu | _ | | | | Trp | | | | | Pro | ggg
Gly
205 | Gly | | _ | 624 |
| Glu | gtg
Val
210 | | | | | | | | | | | | | | | 642 |
| | - 2 | 10. | c 4 | | | | | | | | | | | | | |

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<211> 213

<212> PRT

<213> Cenarchaeum symbiosum

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Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly

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| 65 | i | | | | 70 | | | | | 75 | i | | | | 80 | |
|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|-----|------------|-------------------|-----|
| | | | | | Ser | | | | | Val | | | | | acc
Thr | 288 |
| | | | | Lys | | | | | | | | | | Ala | acc | 336 |
| | | | | _ | aac
Asn | _ | | | - | | _ | _ | Pro | | _ | 384 |
| | | | | | gtg
Val | | | | | | | | | | | 432 |
| | | | | | ata
Ile
150 | | | | | | | | | | | 480 |
| | | | | | acc
Thr | | | | | | | | | | | 528 |
| | | | | | ctc
Leu | | | | | | | | | | | 576 |
| | | | | | ccc
Pro | | | | | | | | _ | | | 624 |
| | | | | | ccg
Pro | | | | | | | | | | | 672 |
| atg
Met
225 | gcc
Ala | ctc
Leu | gac
Asp | gaa
Glu | aga
Arg
230 | tat
Tyr | gcg
Ala | gcc
Ala | ctc
Leu | aag
Lys
235 | agg
Arg | tgc
Cys | Gly | tat
Tyr | gat
Asp
240 | 720 |
| | | | | | tcg
Ser | | | | | | | | | | | 768 |
| | | | | | agg
Arg | | | | | | | | | | | 816 |
| | | | | | ctc
Leu | Asn | | | | | | | | | | 864 |
| | | | | | gag
Glu | | | | | | | | | | | 912 |

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| | Glu | | | | | gac
Asp | | | | | | | | | cgc
Arg
320 | 960 |
|------------|-----|-----|-----|---|---|-------------------|----------|---|---|---|---|---|---|-----|-------------------|------|
| - | _ | , | | _ | _ | gcc
Ala | | _ | | | | | | | aag
Lys | 1008 |
| _ | _ | | _ | | _ | Gly
ggg | _ | | | _ | | _ | _ | | | 1056 |
| | | | | | | gat
Asp | | | | | | | | | | 1104 |
| | | | _ | | | ctc
Leu
375 | | | _ | | | _ | _ | | | 1152 |
| _ | _ | | | _ | _ | gag
Glu | | _ | _ | _ | | _ | _ | | | 1200 |
| | _ | | | - | | aca
Thr | - | | | | | | | _ | | 1248 |
| - | _ | - | | | | gta
Val | | | | | | | | | | 1296 |
| | | | | | | ggc
Gly | | | | | | | | | | 1344 |
| _ | | _ | _ | _ | - | aag
Lys
455 | | | | _ | | _ | | | | 1392 |
| | | | - | | | act
Thr | _ | _ | | | _ | | _ | Arg | _ | 1440 |
| | _ | _ | Leu | _ | | Gly
ggg | | | | | - | _ | - | | | 1488 |
| aag
Lys | | Leu | | | | ttc
Phe | tag
* | | | | | | | | | 1512 |

<210> 66

<211> 503

<212> PRT

<213> Cenarchaeum symbiosum

<400> 66

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Met Glu Thr Ala His Ile Thr Gly Lys Tyr Val Glu Pro Gly Ala Val Glu Arg Arg Asp Tyr Gln Val Gly Leu Ala Glu Gln Ala Ile Arg Glu 25 Asn Cys Ile Val Val Leu Pro Thr Gly Leu Gly Lys Thr Ala Val Ala Leu Gln Val Ile Ser His Tyr Leu Asp Glu Gly Arg Gly Ala Leu Phe 55 Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly 70 75 Arg Ala Leu Thr Ile Ser Asp Ile Thr Leu Val Thr Gly Glu Asp Thr 90 Val Pro Arg Arg Lys Lys Ala Trp Gly Gly Ser Val Ile Cys Ala Thr 105 100 Pro Glu Ile Thr Arg Asn Asp Ile Ala Arg Gly Met Val Pro Leu Glu 120 Gln Phe Gly Leu Val Val Phe Asp Glu Ala His Arg Ala Val Gly Asp 135 Tyr Ala Tyr Ser Ala Ile Ala Arg Ala Val Gly Glu Asn Ser Arg Met 150 155 Ile Gly Met Thr Ala Thr Leu Pro Ser Glu Arg Glu Lys Ala Asp Glu 165 170 Ile Met Gly Thr Leu Leu Ser Lys Ser Ile Ala Gln Arg Thr Glu Asp 180 185 Asp Pro Asp Val Lys Pro Tyr Val Glu Glu Thr Glu Thr Glu Trp Ile 200 205 Lys Val Glu Leu Pro Pro Glu Met Lys Glu Ile Gln Lys Leu Leu Lys 215 Met Ala Leu Asp Glu Arg Tyr Ala Ala Leu Lys Arg Cys Gly Tyr Asp 230 235 Leu Gly Ser Asn Arg Ser Leu Ser Ala Leu Leu Arg Leu Arg Met Val 250 Val Leu Ser Gly Asn Arg Arg Ala Ala Lys Pro Leu Phe Thr Ala Ile 265 Arg Ile Thr Tyr Ala Leu Asn Ile Phe Glu Ala His Gly Val Thr Pro 280 Phe Leu Lys Phe Cys Glu Arg Thr Val Lys Lys Gly Ala Gly Val 295 300 Ala Glu Leu Phe Glu Glu Asp Arg Asn Phe Thr Gly Ala Met Ala Arg 310 315 Ala Lys Ala Ala Gln Ala Ala Gly Met Glu His Pro Lys Ile Pro Lys 325 330 Leu Glu Glu Ala Val Arg Gly Ala Lys Gly Lys Ala Leu Val Phe Thr 345 Ser Tyr Arg Asp Ser Val Asp Leu Ile His Ser Lys Leu Gln Ala Ala 360 Gly Ile Asn Ser Gly Ile Leu Ile Gly Lys Ala Gly Glu Lys Gly Leu 375 380 Lys Gln Lys Lys Gln Val Glu Thr Val Ala Lys Phe Arg Asp Gly Gly 390 395 Tyr Asp Val Leu Val Ser Thr Arg Val Gly Glu Gly Leu Asp Ile 405 410 Ser Glu Val Asn Leu Val Val Phe Tyr Asp Asn Val Pro Ser Ser Ile 425 Arg Tyr Val Gln Arg Arg Gly Arg Thr Gly Arg Lys Asp Ala Gly Lys 440 Leu Val Val Leu Met Ala Lys Gly Thr Ile Asp Glu Ala Tyr Tyr Trp 455 460

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 11e
 Gly
 Arg
 Lys
 Ile
 Thr
 Ala
 Ala
 Arg
 Gly
 Met
 Gly
 Asp
 Arg
 Met

 465
 470
 470
 475
 475
 480

 Asn
 Lys
 Ser
 Leu
 Ala
 Ala
 Gly
 Pro
 Ala
 Pro
 Lys
 Ala
 Ala
 Pro
 Lys

 Lys
 Gly
 Leu
 Gly
 Tyr
 Phe
 490
 490
 495
 495

500

<210> 67

<211> 279

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(279)

<400> 67

atg gcg gac aag ata aag tgc tcg cac ata ctg gta aaa aag cag ggc
Met Ala Asp Lys Ile Lys Cys Ser His Ile Leu Val Lys Lys Gln Gly
1 5 10 15

gag gcg ctc gca gtg caa gag cgc ctc aag gcg ggc gaa aag ttt gga 96
Glu Ala Leu Ala Val Gln Glu Arg Leu Lys Ala Gly Glu Lys Phe Gly
20 25 30

aag ctg gca aag gag ctc tcg ata gac ggg ggc agc gca aag agg gac
Lys Leu Ala Lys Glu Leu Ser Ile Asp Gly Gly Ser Ala Lys Arg Asp

ggc agc ttg ggc tac ttt ggc agg ggc aag atg gta aag ccg ttt gag 192
Gly Ser Leu Gly Tyr Phe Gly Arg Gly Lys Met Val Lys Pro Phe Glu
50 55 60

gat gcc gcg ttc cgc ctg cag gta ggc gag gta tcc gag ccg gta aaa 240 Asp Ala Ala Phe Arg Leu Gln Val Gly Glu Val Ser Glu Pro Val Lys 65 70 75 80

tcc gag ttt ggc tac cac gtg ata aag cgc ctg gga taa 279 Ser Glu Phe Gly Tyr His Val Ile Lys Arg Leu Gly * 85 90

<210> 68

<211> 92

<212> PRT

<213> Cenarchaeum symbiosum

<400> 68

 Met
 Ala
 Asp
 Lys
 Ile
 Lys
 Cys
 Ser
 His
 Ile
 Leu
 Val
 Lys
 Gln
 Gly
 Gly
 Ile
 Leu
 Val
 Lys
 Ala
 Gly
 Gly
 Ile
 Leu
 Lys
 Ala
 Gly
 Glu
 Lys
 Phe
 Gly
 Gly
 Ser
 Ala
 Lys
 Arg
 Asp
 Gly
 Gly
 Ser
 Ala
 Lys
 Arg
 Arg
 Gly
 Lys
 Met
 Val
 Lys
 Pro
 Phe
 Glu

 Asp
 Ala
 Ala
 Ala
 Phe
 Arg
 Leu
 Gly
 Gly
 Lys
 Met
 Val
 Lys
 Pro
 Phe
 Glu

 Asp
 Ala
 Ala
 Ala
 Phe
 Arg
 Leu
 Gly
 Gly
 Gly
 Wal
 Lys
 Pro
 Phe
 Gly

 Asp
 Ala
 Ala
 Ala
 Phe
 Gly
 Wal
 Gly
 Gly
 Gly
 Wal
 Ser
 Gly
 Pro
 Phe
 Gly
 Ala
 Gly
 Gly
 G

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Ser Glu Phe Gly Tyr His Val Ile Lys Arg Leu Gly 85 90

<210> 69

<211> 402

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(402)

<400> 69

atg tct ttg tat ttt acg ata aag acg gcc aac ctg gcc ctg ccc gac

Met Ser Leu Tyr Phe Thr Ile Lys Thr Ala Asn Leu Ala Leu Pro Asp

1 5 10 15

gtg gta aag agg tac aac cac gtc ctg gcg tgc aag agc gag gtg atg 96 Val Val Lys Arg Tyr Asn His Val Leu Ala Cys Lys Ser Glu Val Met 20 25 30

agg gcc gag aag cag atc cag gtg tcc atc tcg tcg ggc ggt ctg 144
Arg Ala Glu Lys Gln Ile Gln Val Ser Ile Ser Ser Ser Gly Gly Leu
35 40 45

gac aag tac gcg gag ctc aag cag cag ttc aac tcg agg ata acc gag
Asp Lys Tyr Ala Glu Leu Lys Gln Gln Phe Asn Ser Arg Ile Thr Glu
50 55 60

ttc tac cgc tcg ata gag gag ctg gag aag acg ggc gtg gtg gtc aag

240

Phe Tyr Arg Ser Ile Glu Glu Leu Glu Lys Thr Gly Val Val Lys

65

70

75

80

agc ata gac gag ggg ctc ctg gac ttt ccc gca aag cgc ttt ggg gac 288 Ser Ile Asp Glu Gly Leu Leu Asp Phe Pro Ala Lys Arg Phe Gly Asp

gac atc tgg ctg tgc tgg aag gtg ggc gag cgc gag atc aag ttc tgg 336
Asp Ile Trp Leu Cys Trp Lys Val Gly Glu Arg Glu Ile Lys Phe Trp
100 105 110

cat gaa aag gac tcg ggg ttt gac gga aga aag ccc ata gag gta agt
His Glu Lys Asp Ser Gly Phe Asp Gly Arg Lys Pro Ile Glu Val Ser
115 120 125

gac gag tca cta gtg tag 402
Asp Glu Ser Leu Val *
130

<210> 70

<211> 133

<212> PRT

<213> Cenarchaeum symbiosum

<400> 70

Met Ser Leu Tyr Phe Thr Ile Lys Thr Ala Asn Leu Ala Leu Pro Asp
1 5 10 15

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Val Val Lys Arg Tyr Asn His Val Leu Ala Cys Lys Ser Glu Val Met 25 Arg Ala Glu Lys Gln Ile Gln Val Ser Ile Ser Ser Gly Gly Leu 40 Asp Lys Tyr Ala Glu Leu Lys Gln Gln Phe Asn Ser Arg Ile Thr Glu Phe Tyr Arg Ser Ile Glu Glu Leu Glu Lys Thr Gly Val Val Lys 70 Ser Ile Asp Glu Gly Leu Leu Asp Phe Pro Ala Lys Arg Phe Gly Asp 90 Asp Ile Trp Leu Cys Trp Lys Val Gly Glu Arg Glu Ile Lys Phe Trp 105 His Glu Lys Asp Ser Gly Phe Asp Gly Arg Lys Pro Ile Glu Val Ser 115 120 Asp Glu Ser Leu Val 130 <210> 71 <211> 879 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (879) <400> 71 atg etc tec tec tgg etg ege gta ata ege gte egg tte etg etc geg 48 Met Leu Ser Ser Trp Leu Arg Val Ile Arg Val Arg Phe Leu Leu Ala teg gtg ata gee gta tea geg gge ett gee ete tee tgg tgg eae gge 96 Ser Val Ile Ala Val Ser Ala Gly Leu Ala Leu Ser Trp Trp His Gly cac gga ata gac geg etc aca geg gca etc acc atg gee gga gtg gee 144 His Gly Ile Asp Ala Leu Thr Ala Ala Leu Thr Met Ala Gly Val Ala get ett cat gea age gtg gae atg ete aac gae tae tgg gae tae aag 192 Ala Leu His Ala Ser Val Asp Met Leu Asn Asp Tyr Trp Asp Tyr Lys 55 cgc ggc ata gat acg aga acc aag agg acc ccg atg agc ggg ggg aca 240 Arg Gly Ile Asp Thr Arg Thr Lys Arg Thr Pro Met Ser Gly Gly Thr 65 ggg gtg ctg cca gag ggc ctg ctg agc ccc cgc cag gtg tac cgc gcc 288 Gly Val Leu Pro Glu Gly Leu Leu Ser Pro Arg Gln Val Tyr Arg Ala 85 90 ggc atc ata tca ctg gtg ctc ggg act gcc gcc gcc gca tac ttt gtg 336 Gly Ile Ile Ser Leu Val Leu Gly Thr Ala Ala Gly Ala Tyr Phe Val 100 105 ate aca acg ggg ecc gte ata get gcg ata etc gge ttt gcg gtg gte 384 Ile Thr Thr Gly Pro Val Ile Ala Ala Ile Leu Gly Phe Ala Val Val 115 120

| | att
Ile
130 | Tyr | | | _ | | | | | | _ | | | | gag
Glu | | 432 |
|-----|-------------------|-----------------------------|-----|------|-----|------|------|-----|------|-----|-------|-----|-------|-------|-------------|---|-----|
| | ctc
Leu | _ | | _ | | | | | | | | | | | | | 480 |
| | cag
Gln | | | | | | | | | | | | | | | | 528 |
| | ggg
Gly | | _ | | | | _ | | | | | _ | | _ | _ | | 576 |
| | gac
Asp | - | _ | _ | | - | | _ | | _ | _ | | | | _ | | 624 |
| | aaa
Lys
210 | | | | | | | | | | | | _ | | | | 672 |
| | tca
Ser | | | | | | | | | | | | | | | | 720 |
| | ctc
Leu | | | | | | | | | | _ | | _ | _ | | | 768 |
| | ctt
Leu | | | | | | | | | | | | | | | ; | 816 |
| | acg
Thr | | Arg | Phe | Ser | Arg | | Ala | | Ala | | Leu | | | | 1 | 864 |
| | ctg
Leu
290 | | | | | | | | | | | | | | | 8 | 879 |
| | <2
<2 | 11>
211>
212>
213> | 292 | rcha | eum | symb | iosu | m | | | | | | | | | |
| Met | | .00> | 72 | | | - | | | n ra | Val | n r a | Dho | I ass | T 011 | 7 1- | | |

Ala Leu His Ala Ser Val Asp Met Leu Asn Asp Tyr Trp Asp Tyr Lys Arg Gly Ile Asp Thr Arg Thr Lys Arg Thr Pro Met Ser Gly Gly Thr Gly Val Leu Pro Glu Gly Leu Leu Ser Pro Arg Gln Val Tyr Arg Ala 90 Gly Ile Ile Ser Leu Val Leu Gly Thr Ala Ala Gly Ala Tyr Phe Val 105 Ile Thr Thr Gly Pro Val Ile Ala Ala Ile Leu Gly Phe Ala Val Val 120 Ser Ile Tyr Phe Tyr Ser Thr Arg Ile Val Asp Ser Gly Leu Ser Glu 135 Val Leu Val Gly Val Lys Gly Ala Met Ile Val Leu Gly Ala Tyr Tyr 150 Ile Gln Ala Pro Glu Ile Thr Pro Ala Ala Leu Leu Val Gly Ala Ala 170 Val Gly Ala Leu Ser Ser Ala Val Leu Phe Val Ala Ser Phe Pro Asp His Asp Ala Asp Lys Glu Arg Gly Arg Lys Thr Leu Val Ile Ile Leu 200 Gly Lys Lys Arg Ala Ser Arg Ile Leu Trp Val Phe Pro Ala Val Ala 215 220 Tyr Ser Ser Val Ile Ala Gly Val Ile Ile Gln Val Leu Pro Val Tyr 230 235 Ser Leu Ala Met Leu Leu Ala Ala Pro Leu Ala Ala Ile Ser Ala Arg 250 Gly Leu Ala Lys Glu Tyr Asp Gly Asp Arg Ile Ile Arg Val Met Arg 265 Gly Thr Leu Arg Phe Ser Arg Thr Ala Gly Ala Leu Leu Val Leu Gly 275 280 Ile Leu Leu Gly 290 <210> 73 <211> 1227 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(1227) <400> 73 ttg agg ccc gcg gct gtg cct aca gca cgg gat att ggc gca gaa cgg 48 Met Arg Pro Ala Ala Val Pro Thr Ala Arg Asp Ile Gly Ala Glu Arg 1 ggc aat ctc aca ctt tgt acc ctt cat aca cat aaa tcc cgc ttg gat 96 Gly Asn Leu Thr Leu Cys Thr Leu His Thr His Lys Ser Arg Leu Asp gtg cgg ctg cgc atg atc agc ggg cat gcc acg gcc gag ggt aca cag 144 Val Arg Leu Arg Met Ile Ser Gly His Ala Thr Ala Glu Gly Thr Gln 40 agg ata gcc gag atg tcc ggc gca cac cat gac aac tac aag gtg gta 192 Arg Ile Ala Glu Met Ser Gly Ala His His Asp Asn Tyr Lys Val Val 55

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| | | - | | | | aac
Asn | | | | | | | | | gac
Asp
80 | | 240 |
|------------|-----|-----|-----|-----|------------|-------------------|-----|-----|-----|------------|-----|-----|-----|-----|------------------|---|-----|
| | | | | | | agg
Arg | | | | | | | | | | | 288 |
| | _ | _ | | | | gtc
Val | | _ | | - | | | | _ | | | 336 |
| | | | | | | gtg
Val | | | | | | | | | | | 384 |
| _ | | _ | _ | | | gac
Asp
135 | _ | | | | | | _ | | | | 432 |
| | _ | | | _ | | gag
Glu | _ | | | - | | | | | - | | 480 |
| | - | - | | _ | | ggc
Gly | | _ | | _ | | | _ | | | , | 528 |
| _ | | | | - | _ | aag
Lys | | | | | | - | _ | | _ | ! | 576 |
| _ | _ | | _ | | _ | aac
Asn | _ | _ | - | | _ | | _ | | | (| 624 |
| | | _ | | | | cag
Gln
215 | | _ | _ | - | | | _ | | | (| 672 |
| Leu
225 | Glu | Gly | Ile | Gly | Glu
230 | gcc
Ala | Phe | Ala | Met | Tyr
235 | Glu | Lys | Met | Arg | Glu
240 | • | 720 |
| | | | | | | tac
Tyr | | | | | | | _ | | | • | 768 |
| _ | _ | | | _ | - | cag
Gln | - | _ | _ | | _ | _ | | _ | | 8 | 316 |
| _ | _ | _ | _ | - | | gj
aga | | | | | | | | | - | 8 | 364 |
| ctg | cca | ttc | aac | cag | tac | ttt | gac | cag | gcc | tac | atg | gta | aag | aac | cag | 9 | 912 |

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| Leu | Pro
290 | | Asn | Gln | туr | Phe
295 | Asp | Gln | Ala | Tyr | Met
300 | | Lys | Asn | Gln | |
|-----|------------|---|-------------------|-----|-----|------------|-----|-----|-----|-----|------------|---|-----|-----|-------------------|------|
| | _ | | ggc
Gly | | _ | | | | _ | | | _ | _ | | ctg
Leu
320 | 960 |
| _ | | | gtg
Val | | | - | _ | _ | | _ | _ | | ~ | | | 1008 |
| | | | ctg
Leu
340 | _ | _ | | | | | | _ | | _ | _ | | 1056 |
| | _ | _ | ttc
Phe | | | | | _ | | | | _ | | - | - | 1104 |
| | | _ | tcc
Ser | _ | _ | | | _ | | | | _ | | _ | - | 1152 |
| | | | att
Ile | | | _ | _ | | | | | | _ | _ | | 1200 |
| | | | tcg
Ser | | | _ | | _ | | | | | | | | 1227 |

<210> 74

<211> 408

<212> PRT

<213> Cenarchaeum symbiosum

<400> 74

Met Arg Pro Ala Ala Val Pro Thr Ala Arg Asp Ile Gly Ala Glu Arg 10 Gly Asn Leu Thr Leu Cys Thr Leu His Thr His Lys Ser Arg Leu Asp 25 Val Arg Leu Arg Met Ile Ser Gly His Ala Thr Ala Glu Gly Thr Gln 40 Arg Ile Ala Glu Met Ser Gly Ala His His Asp Asn Tyr Lys Val Val Asp Gly Leu His Leu Ser Asn Val Gly Met Gly Thr Tyr Leu Gly Asp 75 Ala Asp Asp Ala Thr Asp Arg Ala Val Thr Asp Ala Val Lys Arg Ser 90 Ile Lys Ser Gly Ile Asn Val Ile Asp Thr Ala Ile Asn Tyr Arg Leu 105 Gln Arg Ala Glu Arg Ser Val Gly Arg Ala Val Thr Glu Leu Ser Glu 120 125 Glu Gly Leu Val Ser Arg Asp Gln Ile Phe Ile Ser Thr Lys Ala Gly 135 140 Tyr Val Thr Asn Asp Ser Glu Val Ser Leu Asp Phe Trp Glu Tyr Val 150 155 160

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Lys Lys Glu Tyr Val Gly Gly Val Ile Gln Ser Gly Asp Ile Ser 170 Ser Gly Tyr His Cys Met Lys Pro Ala Tyr Leu Glu Asp Gln Leu Lys 185 Arg Ser Leu Ala Asn Met Asn Val Asp Cys Ile Asp Leu Val Tyr Val 200 His Asn Pro Val Glu Gly Gln Ile Lys Asp Arg Pro Val Pro Glu Ile 215 220 Leu Glu Gly Ile Gly Glu Ala Phe Ala Met Tyr Glu Lys Met Arg Glu 230 235 Ala Gly Arg Ile Arg Tyr Tyr Gly Leu Ala Thr Trp Glu Cys Phe Arg 245 250 Val Ala Glu Gly Asp Pro Gln Ser Met Gln Leu Glu Ala Val Lys 260 265 Lys Ala Lys Asp Ala Gly Gly Glu Asn His Gly Phe Arg Phe Ile Gln Leu Pro Phe Asn Gln Tyr Phe Asp Gln Ala Tyr Met Val Lys Asn Gln Gly Thr Gly Gly Lys Ser Ser Ile Leu Glu Ala Ala Ala Leu 310 315 Asp Ile Gly Val Phe Thr Ser Val Pro Phe Met Gln Gly Lys Leu Leu 330 Glu Pro Gly Leu Leu Pro Glu Phe Gly Gly Leu Ser Pro Ala Leu Arg 345 Ser Leu Gln Phe Ile Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro 360 Gly His Lys Ser Ser Leu His Thr Asp Glu Asn Leu Lys Ile Met Gly 375 380 Val Pro Pro Ile Pro Pro Asp Lys Phe Gly Glu Leu Val Ala Ser Leu 390 Thr Ser Trp Ser Pro Gly Gln Lys 405 <210> 75 <211> 1077 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(1077) <400> 75 atg aac aac egg tte cag gtt atc egg ggg gat gee egg geg gtg etg 48 Met Asn Asn Arg Phe Gln Val Ile Arg Gly Asp Ala Arg Ala Val Leu 1 ccc agg ctt gca aaa aag aat ggc gag cgc ggc agg tac agg ctg gcc 96 Pro Arg Leu Ala Lys Lys Asn Gly Glu Arg Gly Arg Tyr Arg Leu Ala gtc act tcc ccc ccg tat tac ggg cac aga aag tac ggg tcg gat ccc 144 Val Thr Ser Pro Pro Tyr Tyr Gly His Arg Lys Tyr Gly Ser Asp Pro 40 tee gag etg gge cag gag ggg acg eet gat gag tte gte gag gag etg 192 Ser Glu Leu Gly Gln Glu Gly Thr Pro Asp Glu Phe Val Glu Glu Leu 55 60

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| _ | Gly | | | _ | _ | _ | _ | _ | _ | | | - | _ | | agc
Ser
80 | 240 |
|-----|-----|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|------------------|-----|
| | | | _ | | - | gac
Asp | | | | | | | _ | _ | atg
Met | 288 |
| _ | - | | | | | ctc
Leu | _ | | _ | _ | | | | | | 336 |
| | | - | | _ | | tac
Tyr | _ | | | | | | _ | - | | 384 |
| _ | _ | | | _ | _ | gcg
Ala
135 | | | | | _ | | | | _ | 432 |
| | _ | | | _ | | gac
Asp | | - | _ | | _ | _ | _ | | | 480 |
| | _ | _ | _ | | _ | aac
Asn | | _ | _ | | _ | - | | _ | Gln | 528 |
| | | | | | | gac
Asp | | _ | _ | | | | | _ | - | 576 |
| | | | | _ | | ccc
Pro | - | | | | | | _ | | | 624 |
| | | | | _ | | gcc
Ala
215 | | | | _ | | _ | _ | | - | 672 |
| | | | | | | ttc
Phe | | | | | | | | | | 720 |
| | | | | | | ccg
Pro | | | _ | _ | - | | | | | 768 |
| _ | | | | | - | tgg
Trp | | | | | _ | | | | | 816 |
| | | | | | | ttc
Phe | | _ | _ | | - | | | | _ | 864 |
| aag | ttt | gcc | aca | aga | gag | ggc | gac | tat | gtg | ctg | gat | ccg | ttt | gcg | gga | 912 |

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atg ccc gag gga aca cgc tga 1077

Met Pro Glu Gly Thr Arg *

355

<210> 76 <211> 358 <212> PRT <213> Cenarchaeum symbiosum

<400> 76

Met Asn Asn Arg Phe Gln Val Ile Arg Gly Asp Ala Arg Ala Val Leu 10 Pro Arg Leu Ala Lys Lys Asn Gly Glu Arg Gly Arg Tyr Arg Leu Ala 25 Val Thr Ser Pro Pro Tyr Tyr Gly His Arg Lys Tyr Gly Ser Asp Pro 40 Ser Glu Leu Gly Gln Glu Gly Thr Pro Asp Glu Phe Val Glu Glu Leu Ala Gly Val Phe Lys Ser Cys Met Asp Leu Leu Thr Asp Asp Gly Ser 70 Leu Phe Ile Val Ile Gly Asp Thr Arg Arg Arg Arg Lys Leu Met Val Pro His Arg Leu Ala Leu Arg Leu Val Asp Leu Gly Tyr His Phe 105 Gln Glu Asp Ile Val Trp Tyr Lys Lys Asn Ala Leu Ser Gln Ser Ser 120 125 Lys Gln Asn Leu Thr Gln Ala Tyr Glu Phe Val Leu Val Leu Ser Lys 135 Ser Glu Ser Pro Ala Phe Asp Ile Asp Pro Ile Arg Val Gln Gly Asn 150 155 Glu Ala Leu Ser Gly Val Asn Arg Lys Pro Glu Arg Asp Arg Leu Gln 170 Phe Ser Pro Gly Arg Arg Asp Pro Glu Ala Ile Gly Arg Ile Ala Ala 185 Val Ile His Gly Ser Ser Pro Glu Thr Pro Phe Asp Glu Leu Pro Thr 200 205 Thr Glu Glu Ile Ser Arg Ala His Gly Tyr Asp Pro Glu Lys His Cys 215 Pro Thr Cys Tyr Arg Lys Phe Lys Arg His Ala Thr Arg Lys Arg Ile 230 235 Gly Gly His Glu His Tyr Pro Ile Phe Ala Ala Cys Asn Pro Arg Gly 245 250

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| Lys | Asn | Pro | Gly
260 | | Val | Trp | Glu | 11e
265 | | Thr | : Lye | Ala | His
270 | | Gly | |
|-----|---------|------------|-------------|------------|------|-------------|--------------|--------------|------|--------------|------------|------------|------------|------------|-------|-----|
| Asn | Glu | His
275 | | Ala | Val | Phe | Pro
280 | | Asp | Lev | val | Ser
285 | _ | Ile | • Val | |
| Lys | Phe 290 | | Thr | Arg | Glu | Gly
295 | | Tyr | Val | Leu | Asp
300 | | Phe | Ala | Gly | |
| Arg | Gly | Thr | Thr | Gly | Ile | Val | Ser | Ala | Cys | Leu | Lys | Arg | Gly | Phe | Thr | |
| 305 | | | | • | 310 | | | | • | 315 | | _ | • | | 320 | |
| | | Asp | Leu | Tyr
325 | Pro | | Asn | Val | Asp | Arg | | Arg | Arg | Asn
335 | Val | |
| Lys | Asp | Ser | Ala
340 | Asp | | Lys | Leu | Pro | Lys | | Val | Leu | Asp
350 | Gln | Ile | |
| Met | Pro | Glu
355 | | Thr | Arg | | | 3.13 | | | | | 330 | | | |
| | , | 210> | 77 | | | | | | - | | | | | | | ÷ |
| | | 211> | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | |
| | | 212> | | | | | | | | | | | | | | |
| | < | 213> | Cen | arch | aeum | symi | oiosi | um | | | | | | | | |
| | < | 220> | | | | | | | | | | | | | | |
| | < | 221> | CDS | | | | | | | | | | | | | |
| | <: | 222> | (1) | (4 | 468) | | | | | | | | | | | |
| | < | 400> | 77 | | | | | | | | | | | | | |
| atg | cgg | ctg | ccc | cqq | cqc | cga | ctt | aaa | atc | att | qta | gga | tac | ggc | qcc | 48 |
| | | | | | | Arg | | | | | | | | | _ | |
| 1 | 3 | | | 5 | 5 | 3 | | -,- | 10 | | | 1 | 0,70 | 15 | •== | |
| _ | | | | • | | | | | | | | | | | | |
| gca | gat | gca | tta | ccc | acc | tta | tac | acc | acc | caa | gat | caa | cca | cct | tac | 96 |
| | | | | | | Leu | | | | | | | | | | 20 |
| | | | 20 | | | 200 | -1- | 25 | 1114 | 9 | Junp | m 9 | 30 | 110 | Cys | |
| | | | 20 | | | | | 25 | | | | | . 30 | | | |
| age | aca | cac | agt | ata | 220 | a gg | aac | cca | aac | aac | aca | tat | 020 | ata | taa | 144 |
| | | | | | | Gly | | | | | | | | | | 144 |
| JCI | 1111 | 35 | 361 | 116 | WOII | Gry | 40 | PIU | GIY | Gry | MIG | 45 | nis | Mec | тър | |
| | | 33 | | | | | 40 | | | • | | 45 | | | | |
| ata | 227 | 720 | ~ 22 | ++- | ata | ~~~ | ~~~ | ~~~ | 226 | ~~~ | -t- | 222 | at a | | | 100 |
| | | | | | | ggc | | | | | | | | | | 192 |
| IIE | _ | Asp | GIU | Pne | Leu | Gly | Pro | GIY | Asn | гав | | arg | Leu | Leu | Tyr | |
| | 50 | | | | | 55 | | | | | 60 | | | | | |
| | | | | | | | | | | | | | | | | |
| | | | | | | ggg | | | | | | | | | | 240 |
| | TTE | ьeu | Pro | rre | | Gly | Tyr | He | Phe | | GIu | Tyr | Tyr | Pro | Phe | |
| 65 | | | | | 70 | | | | | 75 | | | | | 80 | |
| | | | | | | | | | | | | | | | | |
| | | | | | | tac | | | | | | | | | | 288 |
| Phe | Pro | Trp | Met | Ala | Thr | Tyr | Trp | Trp | Ser | Val | Ala | Leu | Ser | Pro | Pro | |
| | | | | 85 | | | | | 90 | | | | | 95 | | |
| | | | | | | | | | | | | | | | | |
| ata | gtg | CCC | acg | cat | tat | gcc | ggg | gag | gcc | ctg | ggg | cgg | ctg | atc | ggg | 336 |
| Ile | Val | Pro | Thr | His | Tyr | Ala | Gly | Glu | Ala | Leu | Gly | Arg | Leu | Ile | Gly | |
| | | | 100 | | - | | - | 105 | | | • | _ | 110 | | • | |
| | | | | | | | | | | | | | | | | |
| gat | cac | gta | tta | ttt | qqc | atc | acc | aca | aaσ | tac | atc | tat | aca | gca | ata | 384 |
| | | | | | | Ile | | | | | | | | | | 204 |
| | | 115 | | | 1 | | 120 | | _, 5 | - 7 - | | 125 | .,,,, | .110 | **C | |
| | | | | | | | 120 | | | | | 123 | | | | |
| taa | ctc | aac | 2+~ | ac- | a | ~~~ | a t = | a t = | at- | ~ + ~ | | ~~~ | 000 | a+ - | | , |
| -33 | ددو | 990 | acg | gcc | cat | 999 | aca | acc | ctg | ccg | gca | 999 | cgc | CCC | cgg | 432 |

Trp Leu Gly Met Ala His Gly Ile Ile Leu Leu Ala Gly Arg Leu Arg
130 135 140

gga cct agg cag gcg cca cgg acg ggc atc cca tag
Gly Pro Arg Gln Ala Pro Arg Thr Gly Ile Pro *
145 150 155

<210> 78
<211> 155
<212> PRT
<213> Cenarchaeum symbiosum

<400> 78

Met Arg Leu Pro Arg Arg Leu Lys Ile Val Val Gly Cys Gly Ala Ala Asp Ala Leu Pro Ala Leu Tyr Thr Ala Arg Asp Arg Pro Pro Cys Ser Thr Arg Ser Ile Asn Gly Gly Pro Gly Gly Ala Tyr His Met Trp 40 Ile Lys Asp Glu Phe Leu Gly Pro Gly Asn Lys Met Arg Leu Leu Tyr Leu Ile Leu Pro Ile Tyr Gly Tyr Ile Phe Leu Glu Tyr Tyr Pro Phe Phe Pro Trp Met Ala Thr Tyr Trp Trp Ser Val Ala Leu Ser Pro Pro 90 Ile Val Pro Thr His Tyr Ala Gly Glu Ala Leu Gly Arg Leu Ile Gly 105 Asp His Val Leu Phe Gly Ile Thr Thr Lys Tyr Val Tyr Ala Ala Ile 120 Trp Leu Gly Met Ala His Gly Ile Ile Leu Leu Ala Gly Arg Leu Arg 135 Gly Pro Arg Gln Ala Pro Arg Thr Gly Ile Pro 150

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<221> CDS <222> (1)...(1779)

atc ggg ctg gcg gtg gca agg aaa ttt gcc gag aac ggg gcc agc gtg 96

Ile Gly Leu Ala Val Ala Arg Lys Phe Ala Glu Asn Gly Ala Ser Val
20 25 30

48

gta ata ctc gga agg aga aag gag ccc ctc gat gag gca gca gca gag 144
Val Ile Leu Gly Arg Arg Lys Glu Pro Leu Asp Glu Ala Ala Ala Glu
35 40 45

ctc aaa aag ata gcg gaa tct gca ggc tgc ggg gcc tcg atc agg ata 192

| Leu | Lys
50 | Lys | Ile | Ala | Glu | Ser
55 | Ala | Gly | Сув | Gly | Ala
60 | | Ile | Arg | Ile | |
|-----|-----------|-----|-----|-----|-----|-----------|-----|-----|-----|-----|-----------|-------------------|-----|-----|------------------|-----|
| | | | | - | - | | | | | | | acg
Thr | | | ttc
Phe
80 | 240 |
| | | | | | | | | | | | | ctg
Leu | | | | 288 |
| _ | | | _ | | | _ | _ | _ | | _ | | aat
Asn | _ | | _ | 336 |
| | | - | | _ | _ | _ | | | | | | tcc
Ser
125 | | | | 384 |
| _ | | | _ | | _ | _ | _ | | _ | | | aag
Lys | | - | | 432 |
| _ | | _ | | | • | _ | | | | | | cag
Gln | | _ | | 480 |
| | | - | _ | _ | | | | - | | | - | aag
Lys | | | | 528 |
| | | | | | | | | | | | | ata
Ile | | | | 576 |
| | | | | | | _ | | | - | | | tac
Tyr
205 | _ | _ | - | 624 |
| | | | | | | | | | | | | gly
ggg | | | | 672 |
| | | | | | | | | | | | | cta
Leu | | | | 720 |
| | | | | | - | | | | | | | gca
Ala | | | | 768 |
| | | | _ | _ | | - | | | _ | | | aag
Lys | | | _ | 816 |
| | | _ | _ | _ | | _ | | | | | | gcc
Ala
285 | | _ | | 864 |

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| | gcc
Ala
290 | | | | | | | | | | | | | | | 912 |
|------------|-------------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------------|------------|-------------------|-------------------|------------|------|
| | cag
Gln | | | | | | | | | | | | | | | 960 |
| aag
Lys | acg
Thr | gta
Val | aac
Asn | ggc
Gly
325 | cgc
Arg | gta
Val | atc
Ile | ccc
Pro | gcc
Ala
330 | gac
Asp | agg
Arg | gta
Val | ttc
Phe | tac
Tyr
335 | ccg
Pro | 1008 |
| gta
Val | agg
Arg | gcg
Ala | cat
His
340 | gtg
Val | gcc
Ala | aat
Asn | gcc
Ala | gct
Ala
345 | ccg
Pro | cgc
Arg | gtg
Val | ccc
Pro | ccg
Pro
350 | cac
His | gac
Asp | 1056 |
| | tcc
Ser | | | | | | | | | | | | | | | 1104 |
| | gta
Val
370 | | | | | | | | | | | | | | | 1152 |
| | acg
Thr | | | | | | | | | | | | | | | 1200 |
| | atg
Met | | | | | | | | | | | | | | | 1248 |
| | gac
Asp | | | | | | | | | | | | | | | 1296 |
| | ata
Ile | | | | | | | | | | | | | | | 1344 |
| | cta
Leu
450 | | | | | | | | | | | | | | | 1392 |
| | ata
Ile | | | | | | | | | | | | | | | 1440 |
| | ccc
Pro | | | | | | | | | | | | | | | 1488 |
| | atc
Ile | | | | | | | | | | | | | | | 1536 |
| ggc | gcc | gag | agg | gca | agg | gcg | gag | atc | ttc | cgg | ggt | gcg | ctc | agg | ccg | 1584 |

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Gly Ala Glu Arg Ala Arg Ala Glu Ile Phe Arg Gly Ala Leu Arg Pro 520 ctg acg act aca gtc aac cag gag ctc agc gat gtg cta aag tca aac 1632 Leu Thr Thr Val Asn Gln Glu Leu Ser Asp Val Leu Lys Ser Asn 535 540 gtg cgc ctg ttt acc atc ctt ccc ggc agg gcg gac ggg ggc gag acc 1680 Val Arg Leu Phe Thr Ile Leu Pro Gly Arg Ala Asp Gly Glu Thr gat gat tee ege ata tet get gea ate gae tae ttt etg ace eee gag 1728 Asp Asp Ser Arg Ile Ser Ala Ala Ile Asp Tyr Phe Leu Thr Pro Glu 565 get gte teg tee gge gag gte ata tte tge gta gae gag aac agg gge 1776 Ala Val Ser Ser Gly Glu Val Ile Phe Cys Val Asp Glu Asn Arg Gly 580 585 1779 tag <210> 80 <211> 592 <212> PRT <213> Cenarchaeum symbiosum <400> 80 Met Lys Leu Gln Gly Lys Thr Ala Val Ile Thr Gly Ser Gly Thr Gly Ile Gly Leu Ala Val Ala Arg Lys Phe Ala Glu Asn Gly Ala Ser Val Val Ile Leu Gly Arg Arg Lys Glu Pro Leu Asp Glu Ala Ala Ala Glu Leu Lys Lys Ile Ala Glu Ser Ala Gly Cys Gly Ala Ser Ile Arg Ile 55 Phe Ala Gly Val Asp Val Ala Asp Glu Ser Ala Ile Thr Lys Met Phe Asp Glu Leu Ser Ser Ser Gly Val Thr Val Asp Ile Leu Val Asn Asn 90 Ala Gly Val Ser Gly Pro Val Thr Cys Phe Ala Asn Asn Asp Leu Glu 100 105 Glu Phe Arg Gly Ala Val Asp Ile His Leu Thr Gly Ser Phe Trp Thr 120 125 Ser Arg Glu Ala Leu Lys Val Met Lys Lys Gly Ser Lys Ile Val Thr 135 Met Thr Thr Phe Phe Ala Glu Glu Arg Pro Leu Glu Gln Arg Pro Tyr 150 Arg Phe Arg Asp Pro Tyr Thr Thr Ala Gln Gly Ala Lys Asn Arg Leu 170 165 Ala Glu Ala Met Ser Trp Asp Leu Leu Asp Arg Gly Ile Thr Ser Ile 185 Ala Thr Asn Pro Gly Pro Val His Ser Asp Arg Ile Tyr Lys Thr Val 200 Tyr Pro Arg Ala Ala Leu Glu Phe Val Arg Val Ser Gly Phe Glu Asp 220 215 Leu Gln Pro Glu Glu Val Glu Val Ala Gly Gly Arg Leu Ile His Leu

235

230

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```
Leu Gly Ala Asp Asp Asp Ala Arg Lys Lys Gly Ile Ala Glu Ala Ala
                                   250
Glu His Phe Ala Lys Leu Lys Pro Val Asp Pro Ala Lys Leu Glu Ala
                               265
Thr Leu Asp Ala Leu Leu Ala Lys Ile Lys Gly Ile Ala Glu Lys Ile
                           280
Gln Ala Asn Thr Ala Arg Met Ile Pro Asp Gly Glu Phe Leu Ser Gln
                      295
Asp Gln Val Ala Glu Thr Val Leu Ala Leu Cys Asp Asp Lys Met Ala
                   310
                                      315
Lys Thr Val Asn Gly Arg Val Ile Pro Ala Asp Arg Val Phe Tyr Pro
               325
                                  330
Val Arg Ala His Val Ala Asn Ala Aro Arg Val Pro Pro His Asp
           340
                              345
Tyr Ser Gly Gly Cys Val Leu Phe Met Ile Asp Ala Ala Asp Asp Arg
                           360
Asp Val Glu Arg Ala Thr Ala Leu Ala Ser His Val Glu Ser His Gly
                       375
Gly Thr Ala Val Cys Ile Val Ser Glu Asp Ser Pro Arg Ala Ala Lys
                  390
                           395
Glu Met Ile Ala Ser Lys Phe His Ser His Ala Ser His Ile Asp Lys
                    410
Val Asp Glu Ile Asn Arg Trp Leu Ser Ala Ala Ser Thr Lys Ile Gly
                              425
Pro Ile Ser Ala Val Val His Leu Ser Gly Arg Met Pro Lys Ser Gly
                          440
Ser Leu Met Asp Leu Ser Arg Lys Glu Trp Asp Ala Leu Val Asp Arg
                      455
                                          460
Phe Ile Gly Thr Pro Ala Ala Val Leu His Arg Ser Leu Glu His Phe
                  470
                                      475
Ala Pro Gly Gly Arg Lys Asp Pro Arg Leu Phe Lys Gly Lys Ser Gly
                                  490
Val Ile Val Ile Ile Gly Pro Asp Leu Pro Ala Gly Lys Lys Ala Ser
                              505
Gly Ala Glu Arg Ala Arg Ala Glu Ile Phe Arg Gly Ala Leu Arg Pro
                          520
Leu Thr Thr Thr Val Asn Gln Glu Leu Ser Asp Val Leu Lys Ser Asn
                      535
                                          540
Val Arg Leu Phe Thr Ile Leu Pro Gly Arg Ala Asp Gly Gly Glu Thr
Asp Asp Ser Arg Ile Ser Ala Ala Ile Asp Tyr Phe Leu Thr Pro Glu
              565
                                  570
Ala Val Ser Ser Gly Glu Val Ile Phe Cys Val Asp Glu Asn Arg Gly
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<211> 40

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<213> Cenarchaeum symbiosum

<220>

<221> TATA_signal

<222> (11) . . . (16)

<400> 81

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       <220>
       <221> TATA_signal
       <222> (11) ... (16)
       <400> 82
aagctaaact tttaattggg atccggcgag ccggcgcgtg
                                                                          40
      <210> 83
      <211> 41
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA signal
      <222> (11)...(16)
      <400> 83
ggaaactttg attatacggg cgtgctgccc cggggcccat g
                                                                          41
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      <211> 41
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11)...(16)
      <400> 84
ggaaactttg attatacggg cgtacattcc cggggcccat g
                                                                          41
      <210> 85
      <211> 42
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA signal
      <222> (11) . . . (16)
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aaggcaaggt aataatagcc tgccgtctgt aacggccgta tg
                                                                          42
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      <211> 42
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11)...(16)
      <400> 86
acggcaaggt aataatagcc tgccgtccgt acctgccgta tg
                                                                         42
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      <222> (11) ... (16)
      <400> 87
catggaacta gatattaacc ggttccgcgg atcccatgca tg
                                                                           42
      <210> 88
      <211> 42
      <212> DNA
      <213> Cenarchaeum symbiosum
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      <221> TATA signal
      <222> (11) ... (16)
      <400> 88
catggaacta gataataacc ggtcccgcgg gtacaatgca tg
                                                                           42
      <210> 89
      <211> 43
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      <220>
      <221> TATA signal
      <222> (11)...(16)
      <400> 89
ataccgagaa gttatagcag ggtatggaat gtgcgcgcgc atg
                                                                           43
      <210> 90
      <211> 43
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11) . . . (16)
      <400> 90
agcacgacaa gttatagcag ggtacaaagg agcagcgcac atg
                                                                          43
      <210> 91
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      <212> DNA
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      <220>
      <221> TATA_signal
      <222> (11) . . . (16)
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```
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atccgccctg attaaattat ggggggagcg gcctgctgcc gtg
                                                                          43
      <210> 92
      <211> 43
      <212> DNA
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      <220>
      <221> TATA_signal
      <222> (11) ... (16)
      <400> 92
atcoggootc attaaattac ggggggtaca acctgctgcc gtg
                                                                          43
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      <212> DNA
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      <220>
      <221> TATA_signal
      <222> (11) ... (16)
      <400> 93
cetteataca cataaateee gettggatgt geggetgege atg
                                                                          43
      <210> 94
      <211> 43
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11) ... (16)
      <400> 94
acttcataca cataaatccc gcctgaacgg tcgtccgcgc atg
                                                                          43
      <210> 95
      <211> 43
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA signal
      <222> (10) ... (15)
      <400> 95
ggcatatacc ataatatgcc gggcggtggc accatggccg ttg
                                                                          43
      <210> 96
      <211> 43
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
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<222> (11)...(16)
       <400> 96
ccgcatatac cataatatgc cgggcggggg caggctgccc gtg
                                                                           43
      <210> 97
      <211> 44
       <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA signal
      <222> (11) ... (16)
tgtacgaaac cataaaacaa caggccgcgt cagggccgcg cgtg
                                                                          44
      <210> 98
      <211> 43
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11) ... (16)
      <400> 98
gggtagaaac cataaaacaa caggccgcgg cagggcgcgc gtg
                                                                          43
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      <211> 42
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      <221> TATA_signal
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acacgcagta taaacggggg cccgggcggc gcgtatcaca tg
                                                                          42
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      <211> 43
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      <220>
      <221> TATA_signal
      <222> (11) . . . (16)
      <400> 100
atacacgtgg tataaacaga ggccggacgg cgcggaccac atg
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gcgatagtta tttaaaacta ggatgccgat cacggatcgt ccca
                                                                          44
       <210> 102
       <211> 44
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      <400> 102
gcgatagtta tttaaaacta ggatgccggg cacccgtcgt ccca
                                                                          44
      <210> 103
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      <212> DNA
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      <222> (11) ...(16)
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ccgggccccg gttaaaatag cgcacgggcg gatcctgacc aatg
                                                                          44
      <210> 104
      <211> 45
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11) ... (16)
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ccgggccccg gttaaaatag agtgcggccg ggcaccggat caatg
                                                                          45
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      <211> 51
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA signal
      <222> (11)...(16)
      <400> 105
gcgtcgatag aataaatacg cgcaggggc cccgtggcgc gatcgcccgt g
                                                                         51
      <210> 106
      <211> 47
      <212> DNA
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<213> Cenarchaeum symbiosum
       <220>
       <221> TATA_signal
      <222> (11) ... (16)
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gcgtcgatag aataaatacg cgcggggccg cggtgcgatc gcccgtg
                                                                          47
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      <211> 60
      <212> DNA
      <213> Cenarchaeum symbiosum
      <220>
      <221> TATA_signal
      <222> (11) . . . (16)
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atttcaacta cataaatgcc tagttacgca gaaatagcaa acgacgtact tcgactaatg
                                                                         60
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      <221> TATA_signal
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acttcaacta cataaatgcc tagctacgca gaaatatcaa acaaagtact tcgactaatg
                                                                         60
      <210> 109
      <211> 67
      <212> DNA
      <213> Cenarchaeum symbiosum
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      <221> TATA signal
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acggcaggct attattacct tgccttgcgt tgtatagtat gccttatgcg gggtgcggca
                                                                         60
ggggatg
                                                                         67
      <210> 110
      <211> 66
      <212> DNA
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      <220>
      <221> TATA_signal
      <222> (11)...(16)
      <400> 110
acggcaggct attattacct tgccgtgtgt acagggcatg ccggatgagg gggcctgccg
                                                                         60
ggagtg
                                                                         66
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All and the second

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<210> 111
       <211> 121
       <212> DNA
       <213> Cenarchaeum symbiosum
       <220>
       <221> TATA_signal
       <222> (11) . . . (16)
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ctacaacgat tttaagtcgg cgccggggca gccgcataga atgtgtatga cccgtaggat
                                                                          60
egegeggeee geetgetgeg eagatetgte egteeageet gatgtgggge aggeaacatg
                                                                         120
а
                                                                         121
       <210> 112
       <211> 98
       <212> DNA
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ctacaaagat tttaagacgg cgcgggtgcc gcggtacaag atgaatacga cttgtcggat
                                                                         60
cgcgcagggg cagatggatg gcacgggggc ctatcttg
                                                                         98
      <210> 113
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      <212> DNA
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      <220>
      <221> TATA signal
      <222> (11) ...(16)
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teggegatgg tttatatgcc catggaeggg cegateegat egtacgtgae gcaagagegg
                                                                         60
cgcttgcgat gaatgcatgg tattgtacca tattgtgatt cgctggcctc cagttacgca
                                                                        120
cacagaatga gggtatgatc gaagggtcat atctgagatg tgaagattat gtgcattctg
                                                                        180
ttcaattcca aaagtacaag cgtacttaac aaaaaaaaa taatccaatt atgaat
                                                                        236
      <210> 114
      <211> 235
      <212> DNA
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      <220>
      <221> TATA signal
      <222> (11) . . . (16)
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                                                                        60
cgcttgcgat gaagccatgg tattgtacca ttttgtgatt cgcaggcctc cagttacgca
                                                                       120
cacagaatga ggatctgatc gaagggtcat atctgagatg tgaagattat gtgcattccg
                                                                       180
ttcaattcca aaagtacagg cgtactttga aaaaaaaaat aatccaaata agaat
                                                                       235
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```
<210> 115
       <211> 20
       <212> DNA
       <213> Artificial Sequence
       <220>
       <223> Oligonucleotide
       <400> 115
 gtgctccccc gccaattcct
                                                                          20
       <210> 116
       <211> 15
       <212> DNA
       <213> Artificial Sequence
       <220>
       <223> Oligonucleotide
       <400> 116
ctttccctca cggta
                                                                         15
      <210> 117
      <211> 19
      <212> DNA
      <213> Artificial Sequence
      <220>
      <223> Oligonucleotide
      <400> 117
ctattgccgt ctttacacc
                                                                         19
      <210> 118
      <211> 21
      <212> DNA
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      <220>
      <223> Oligonucleotide
      <400> 118
gaateegeee eegaetatet t
                                                                         21
      <210> 119
      <211> 18
      <212> DNA
      <213> Artificial Sequence
      <220>
      <223> Oligonucleotide
      <400> 119
catggcttag tatcaatc
                                                                         18
      <210> 120
      <211> 23
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<212> DNA

| <213> Artificial Sequence | |
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| <222> (3) (3) | |
| <223> I | |
| <221> modified_base | |
| <222> (12) (12) | |
| <223> I | |
| <400> 120 | 23 |
| acntacaacg gngacgaytt tga | |
| <210> 121 | |
| <211> 21 | |
| OLO DNA | |
| <212> Artificial Sequence | |
| <220> | |
| <223> Oligonucleotide | |
| <400> 121 | 21 |
| caccccgaar tagttyttyt t | |
| <210> 122 | |
| <211> 19 | |
| O. C. DNA | |
| <213> Artificial Sequence | |
| <220> | |
| <223> Oligonucleotide | |
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